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THE RECOGNITION OF THE POISONOUS SERPENTS OF NORTH AMERICA.*

By Howard A. Kelly, *Professor of Gynecology The Johns Hopkins University and Gynecologist-in-Chief The Johns Hopkins Hospital.*

I have felt an interest in snakes since boyhood, but the more practical duties of life have prevented my following this penchant for over twenty years. It becomes now, however, my pleasure to brush up the forgotten lore in order to put before you certain facts I think you should all master before graduation. If our medical curriculum were not already crowded, I should urge a brief course of lectures year by year, followed by an examination, upon the subject of the various poisonous insects and animals and their antidotes; for to whom shall the victim of injuries sustained in this way appeal for accurate information as to the danger from a given bite or sting and the identification of the species causing it, as well as the proper treatment, if not to you?

I shall speak briefly this evening of one group of poisonous animals—the snakes; and it shall be my effort to impress upon you such details of their structure that you shall be able to decide with certainty whether a given species submitted for your examination is or is not poisonous.

In classifying and identifying the various species you will find somewhat useful, although often confusing, Baird and Girard's Catalogue of North American Reptiles in the Museum of the Smithsonian Institution, Part I, Serpents, published in 1853; Jordan's Manual of the Vertebrates in the Northern United States, 1899, is most valuable, and Leonhard Stejneger's work on the Poisonous Snakes of North America is indispensable; the last-named work published by the government for the Smithsonian Institution really ought to be in the hands of every physician in the land. Dr. Yarrow, of Washington, one of our most eminent authorities, has written numerous treatises, including an article in Wood's Reference Handbook of the Medical Sciences. Other works are a Catalogue of Snakes in the British Museum, in three volumes, by Boulenger, London, 1893; Herpetologia Europæa, by E. Schreiber, Braunschweig, 1875, and Deutschland's Amphibien und Reptilien, by B. Dürigen, Magdeburg, 1897.

Snakes are reptiles distinguished from batrachians (the frog family) by the fact that they undergo no metamorphoses and do not pass through a tadpole stage of existence. Snakes either lay eggs and are oviparous, or they produce their young living from eggs hatched but a short time before inside the mother, when they are ovoviviparous; they are distinguished from the lizards by possessing widely dilatable mandibles and the fact that the head-bones are united by ligaments, while they possess no limbs or shoulder-girdle, and have no eyelids

*An address with a demonstration to the Graduating Class in the Medical School, before the Johns Hopkins Hospital Medical Society, November 6th, 1899.

and no external ear or tympanum. In boas there are little rudimentary hind limbs.

The body of the snake is covered with scales arranged in rows down the back and on the sides; large transverse overlapping scales in a single row cover the belly. The head, as in the lizards, is covered with a series of large plates which are constant in their arrangement in the same species, and therefore important aids in classifying and identifying species.

One might suppose from this statement that nothing would be easier than to determine whether or not a given animal is a snake; there are, however, several little animals which are popularly considered as snakes which belong in other orders. I show you here for example an animal, the Amphiuma means, widely known as the "Congo snake," and looking much like an eel, but able to live a long while out of the water. On close inspection you will discover four short rudimentary limbs with little toes, and on each side of the neck there is a spiracle. In walking the Amphiuma uses these feet, useless as they appear to be, as I have frequently had occasion to observe in this specimen which I kept alive for some time. It is one of the tailed batrachians, and therefore much more closely allied to the frogs than to snakes.

While the Amphiuma comes from a lower order than the snakes and much resembles a fish, I show you here on the other hand a beautiful lively little animal everywhere known as a "glass snake," the Ophisaurus ventralis, belonging to the family of the lizards, which has a long cylindrical snake-like body closely covered by overlapping scales; it is over two feet in length, without any trace of limbs, and necessarily adopts the same mode of progression as snakes. The Ophisaurus is, however, distinguished from the snake, upon closer examination, by solidity of the head, the well-defined ear-openings near the angle of the jaw as well as the distinct eyelids. It has also this distinguishing characteristic: the vent lies about one-third of the length of the animal back of the head instead of nearer the tail. I received this fine specimen from Dr. John C. Rodman, of Wilmington, N. C., who writes me that its captor told him that if struck with a whip it would break into a number of pieces, which if let alone will come together again in the course of an hour.

The Ophisaurus is a gentle and perfectly harmless little creature, and so is the Congo snake, which feeds on worms and crawfish. There is in the whole world no known poisonous member either of the batrachians or of the lizard family, popular superstition to the contrary, with the single exception of these two large lizards which I here show you, the Gila monsters (Heloderma suspectum), received from Dr. John S. Pearce, of Albuquerque, N. M.

They are so sluggish that I have never seen them attempt to bite; the most they have done in the couple of months they have been in my possession has been to crawl slowly around their cage and eat the eggs on which I feed them.

Among the true snakes, the Ophidians, we must distinguish carefully those which are poisonous from those which are not, and not be misled by a widely prevailing notion that all snakes are poisonous and ought therefore to be destroyed. As an example of the misfortune of ignorance on this head, I may cite the experience of a prominent Baltimore doctor who, while fishing in one of the rivers near town and letting his hand hang in the water, was bitten by a harmless water-snake (probably Tropidonotus sipedon), and for fear that he was poisoned he immediately consumed a large amount of whisky to act as an antidote.

No ophiologist I know of takes the ground that poisonous snakes should not be destroyed, but the ignorance which leads people to destroy all snakes alike does not tend, as they think, to promote the extermination of the poisonous species, but in fact actually tends to preserve them, as their worst enemies are some of their own congeners of the harmless species, such as the black and the king-snakes (see Fig. 1).

The ignorant prejudice which leads people to destroy snakes indiscriminately tends further to seriously disturb the balance of nature by favoring the increase of the small animals upon which they naturally feed, such as toads and frogs and particularly the destructive field-mice which are consumed by thousands.

With a view, therefore, of giving you this information, which may at any time become a matter of vital importance to your patients, as well as with an earnest desire to save the innocent species, I shall now point out to you certain differential points between the poisonous and non-poisonous forms by which they may be most readily distinguished.

Fortunately the poisonous species are few in number and readily distinguished after one has once carefully noted some of their characteristic marks.

The poisonous snakes of this country, with the single exception of the little harlequin-snake (Elaps) of Florida and the South, belong to the group known as "pit-vipers," that is to say, they possess a curious conspicuous blind depression, which is a prominent anatomical characteristic in the fore part of the head over the upper lip between the eye and the nostril in what is known as the loral region. This pit is hollowed out in the thick short superior maxillary bone, which here has the sole function of supporting the poison-fangs. Zoölogists have never been able to determine the function of the pit; Professor Leydig, finding it supplied with a large nerve not unlike the nerve of the eye and of the ear, has concluded that it is the organ of a sixth sense. The pit-vipers differ from the harmless snakes further in that their heads are triangular, with massive maxillary development expressive of great muscular power in the jaw; they have fewer large scales on the head, and a greatly increased number of small scales taking their place, giving the head more of a warty appearance. The snake is thicker in proportion to its length and has a shorter tail, and the dorsal scales are keeled, making the surface conspicuously rough. The pupil is elliptical. If the mouth is opened, the usual number of small teeth are seen in the lower jaw, while, above, a row of recurved short teeth is seen well in towards the centre of the head; these are the palatal teeth, while just outside of these, under the lip and well toward the front are two long mucous folds which hang like veils over the powerful recurved fangs which lie concealed with a number of smaller reserve fangs behind them. If the snake is living, as in the case of the copperhead which I now show you, he is apt upon touching the fangs to throw one or both forward, projecting and erecting them as in striking; further if the edge of a saucer or a watch-glass such as I hold

here is placed under the fang, a convulsive movement may be started by which the animal endeavors to thrust his fangs into the object and then rotates the maxillary bone inwards so as to bring them violently towards the gullet with the ejection of a few drops of the clear yellow poison. In a large diamond-back rattler a teaspoonful of poison may be ejected. For a description of the mechanism see S. Weir Mitchell's report to the Smithsonian Institution.

The poison-fangs are shed from time to time; I show you one dropped a few days ago in my library by this large banded rattlesnake, which is also just about to shed the opposite fang, which I now remove.

I will now characterize the pit-vipers a little more closely by stating that there are three genera with somewhere about 18 species, and all but two of these belong to the rattlesnakes, which are easily recognized by the caudal appendage.

The genera are Agkistrodon, Sistrurus and Crotalus.

The two snakes to which I now call your attention are the copperhead and the water-moccasin, both belonging to the same genus, Agkistrodon, and known respectively as Agkistrodon contortrix and Agkistrodon piscivorus.

The distribution of the copperhead (Agkistrodon contortrix), says Stejneger, "in a general way is coëxtensive with that of the banded rattlesnake (Crotalus horridus), though as a rule it does not extend quite so far north. As a compensation it goes considerably farther south in the western portion of its range, extending into the southern part of Texas."

I exhibit here two well-developed adult copperheads, received from Dr. Rodman, of Va., and Dr. Goss, of Georgia. The color as you see is a light chocolate, with wave-like dark alternating patches on the sides, the belly is yellowish; there are twenty-three rows of scales from side to side, all strongly carinated. The copperhead I think the handsomest of all our snakes. The arrangement of the scales on the head can be seen in the drawing made by Mr. Becker; the particular point of difference here between the copperhead and the moccasin lies in the presence of the loral plate in the copperhead, and its absence in the moccasin (see Figs. 2 and 3).

Although vicious and usually striking without warning, the copperhead is not so dangerous as the rattlesnake when the poison is taken volume for volume; its bite is also less liable to prove fatal, as the snake rarely exceeds three feet in length, and the amount of poison available at any given time is much less than in the larger rattlesnakes.

The moccasin (Agkistrodon piscivorus) is distinctively a water-snake, and is of dark greenish brown color, sometimes almost black, variegated by a series of darker but indistinct bars. The twenty-five rows of dorsal scales are carinated. The lower wall of the eye is bordered by the third labial plate, counting back from the rostral in the middle of the upper jaw (see Figs. 4 and 5). The loral plate is absent. The moccasin, or cottonmouth, as it is often called, can easily be distinguished from other snakes by the following marks: In the first place, its general configuration broad in proportion to length, the triangular head, the thick jaw, suggest at once that it belongs to the vipers; a closer examination shows that it possesses the characteristic pits between the eyes and the nostrils, settling the fact that it is a pit-viper. It then only remains to distinguish it from the group of rattlesnakes on the one hand, which is easily done by the absence of the characteristic caudal appendage; and on the other hand from the copperhead, its closest ally, and this is easily done by the remarkable difference in color, the copperhead being of a lustrous copper-color, while the markings of the water-moccasin are all more or less obscure, and it possesses no beauty of coloration.

A further distinguishing and characteristic mark is a narrow yellowish white line beginning below the eye and passing backward and crossing the angle of the mouth at the seventh labial, as shown in Mr. Becker's drawing.

Although there is everywhere felt a wholesome dread of the moccasin, and Jordan calls it "the most dangerous of our snakes," I know of but one recorded fatality. Dr. J. R. Hopkins, of Hopkins, S. C., tells me that the cattle in his country are sometimes bitten when drinking in the branches and return with their heads much swollen.

I will be brief in considering the rattlesnakes, so easily recognized by their specific appendage, the rattle at the end of the tail. There are two genera, Sistrurus and Crotalus; Sistrurus, at the time I last took an active interest in snakes, was known as the little rattlesnake, or the prairie-rattler, belonging to the genus Crotalophorus or Caudisona. The two species, inhabiting the United States, recognized by Stejneger, are the massasauga (Sistrurus catenatus), and the ground-rattlesnake described by Linnaeus (Sistrurus miliarius). Although there is a popular dread of these animals, there is reason to question whether their bite is ever fatal.

In the form of the head and its broad plates, the snakes of this genus are more nearly allied to the harmless Colubers than any of the Crotalids.

I have here three living rattlesnakes representing two species: the first two are specimens of Crotalus horridus, the banded rattlesnake; one of these, so black as to scarcely show any markings, comes from central Pennsylvania, while the larger snake, 50 inches in length and 7¼ in circumference, is a beautiful specimen from Dr. Goss, in Georgia; he has buff, finely mottled background, crossed at frequent intervals by rich velvety zigzag lines from two to three scales in breadth. In order to emphasize the remarkable contrast between these poisonous vipers and some of the harmless snakes, which I shall produce presently, note that of the entire 50 inches but 4 inches is tail. All the rattles of this larger snake have been lost, so that when he vibrates his tail as now there is no sound whatever unless the end of the tail strikes a hard or dry surface; this disposes of the common notion that the number of rattles is any indication of the age of the animal; note also, as I open the mouth, that the fang of one side has been shed, and the other is just ready to drop into the watch-glass which I hold under it.*

The curious pit, so distinctive of our vipers, is well defined and measures 5 millimeters in depth.

I also show you here another beautiful Crotalus, received from Oklahoma, through Mrs. J. W. Putts of this city, 43½

* Two large new fangs were found in position, ready for service, two weeks later.

inches long, powerfully built in proportion to his length, with six rattles which are vigorously agitated at the slightest provocation. I have had some difficulty in identifying the species. Dr. Stejneger, of Washington, however, decides that it is the prairie-rattlesnake (Crotalus confluentus), which, in some specimens, shows more green The ground color, in remarkable resemblance to the sage-bush of the prairies, is of a yellowish green broken by a series of dorsal oblong blotches which are more or less quadrangular in form, edged by a lighter streak. On the sides between the blotches and belly-scales there are two rows of dark spots, which coalesce in the tail region with the blotches so as to form half rings; the head has the characteristic form, is markedly triangular, with powerful jaws, and looked at from above it is covered with tuberculate and carinated scales; (see Fig. 6) the only large scales seen are the strongly developed superciliaries which project far over the eye, each of which is traversed by a fine yellow line bifurcating at its median end; looked at from the side the head-scales are all larger and there are two striking yellowish streaks extending from the angles of the eye back to the angle of the mouth. The large rostal scale is marked by a white line on the margins.

The harmless snakes, the Colubers, are much more abundant than the poisonous varieties just mentioned and can easily be distinguished from them even upon a superficial examination of their slender form, the large scales covering the head, the smooth scales covering the body in many species, together with the absence of the maxillary pit. When the mouth is opened two long rows of small teeth are found in the upper jaw attached to the palatal and the maxillary bones. The numerous small curved maxillary teeth on the long maxilla replace the single large fang on the short quadrate bone found in the vipers. Many people are afraid of handling the Colubers, dreading the bite and an extensive lacerated wound. The fact is that the bite of the largest of them, 5 or 6 feet long is quite insignificant. I have myself twice been bitten recently by a large blacksnake and by this large, powerful water-snake; a few trifling punctures and a few drops of blood were the only result, and the wound healed as though the skin had been pricked by a needle. Any one of these snakes will attempt to make his escape when encountered, but most of them will fight when cornered, or when picked up for the first time. The blacksnake particularly deserves his reputation as a fighter; one which I have been keeping in the country in a large vivarium is always ready to fight me every time I enter.

As an example of a fine Coluber here is a corn-snake (Callopeltis guttatus) looking much like a blacksnake, 55 inches long, with 27 rows of scales across the back, and on close inspection those towards the middle are found to be faintly keeled while the lateral ones are smooth. The usual coloration of this snake is a reddish-brown color with a row of blotches down the back. In this specimen the color is almost uniformly a dull reddish black. Closely allied to this is the pilot-snake, which is one of our largest serpents, measuring six feet or more.

Here is another beautiful, graceful, harmless snake, one of the slenderest of our large snakes, known as the coachwhip (Masticophis flagelliformis), received from Dr. Goss in Georgia. This specimen is 79¾ inches in length. The fore part of the body, as you observe, is jet black above and below, and shades gradually backward into a dull white; the tail is particularly beautiful, as the smooth scales there become broader and margined with a darker streak marking each wart and giving it a tesselated appearance. The eye of this snake is large and handsome, while the pupil is surrounded by a reddish iris which gives it, under the overhanging superciliary, a particularly striking lustrous appearance, not unlike the imitation snakes made in the form of bracelets by the jewelers. I show here the arrangement of the scales of the head, giving the peculiar elongate vertical plate with the large superciliaries and occipitals. Note that although the length of the jaw as measured to the commissure is only 33 mm., the real length is 40 mm., as the angle of the jaw lies well behind the commissure, showing that the capacity to swallow is much greater than would at first sight seem possible.

I shall not pause to dwell on the specific characters of a number of snakes I here show you which are manifestly harmless; among them are the young of the hognose viper (Heterodon simus), the exquisite slender little green snake (Opheodrys aestivus) from Georgia, and a little Storeria Dekayi of a dim or slate color, with small dark spots on the back, only ten inches in length and three-sixteenths of an inch in diameter.

Most important is it that you should learn to recognize and differentiate certain perfectly harmless snakes which through ignorance have acquired a bad reputation. Here, for example, is a full-grown hognosed viper, or spreading, puffing or blowing adder (Heterodon) as it is often called, one of our most valuable serpents in the destruction of field-vermin, found over a wide geographical range, and everywhere in ill-repute as deadly poisonous, and yet perfectly harmless and most gentle and easily tamed. When first alarmed this snake flattens himself out until the upper part of his body and his head are spread out like a thin skin and bearing a remarkable resemblance to the hood of a cobra. He then draws in wind and forces it out with a loud hissing sound, presenting on the whole a most threatening and forbidding aspect. Even if you were to pick him up and he bit you, the bite would not amount literally to more than the pricking of "a row of pins."

Of this "viper" there are two species, one blackish and the other with considerable yellow or reddish in the background, respectively Heterodon niger and Heterodon simus, both of which are easily distinguished by the "hognose," or retroussée nose, formed by the projecting turned-up rostral scale. (See Mr. Becker's drawing, Figs. 7 and 8.)

Another snake with a bad reputation is this one, which came to me from Alabama, labeled "orange-bellied moccasin," "deadly poisonous," which is really only a large water-snake (Tropidonotus, or Natrix) found abundantly everywhere and not resembling in the least any form of poisonous serpent except in his natural vicious, ugly disposition. He is confused with the true moccasin (Agkistrodon) because he is dull in color and found about the water in the same localities, and is rough-backed with prominent carinated scales; but a glance at the head, which is elongate and colubriform, the

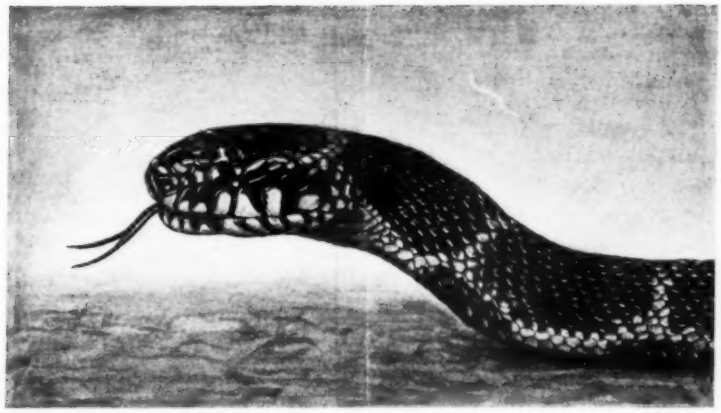

FIG. 1

Ophibolus getulus, king snake, or chain snake, one of the most beautiful of our harmless snakes, found through the South and as far north as Maryland, invaluable in the destruction of vermin. The markings are black and white or yellowish. The loral scale is seen between the anteorbital and the nasal. The absence of a pit and the form of the head show that this is not a poisonous snake.

FIG. 2

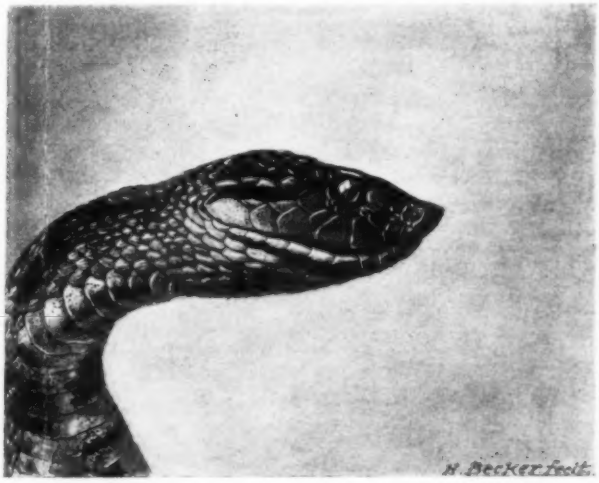

FIG. 3

Agkistrodon Contortrix, Copperhead, a common pit viper of wide distribution, belonging to the same genus as the moccasin. The most marked difference in the scutellation of the head lies in the presence of the loral scale, between anteorbital and nasal in the copperhead, and its absence in the moccasin.

FIG. 4.

Agkistrodon piscivorus, true moccasin. The head is large and triangular with massive jaws. The plates and scales are large. The pit is well shown on a line joining the nostril with the lower border of the eye. There is no loral scale between the nasal and the anteorbitals. The markings on the side of the head are characteristic. Those on the body seen in Fig. 4 are often obscure.

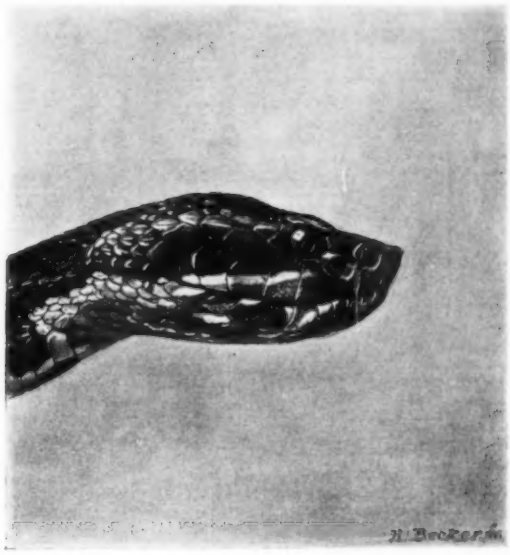

FIG. 5.

Crotalus confluentus, "Prairie rattlesnake," from Oklahoma, one of the group of rattlesnakes with square blotches on the back.

Note the absence of large scales on top of the head, with the exception of the projecting superciliaries. The pit is seen below and behind the nostril. The arrangement of the lines on the head is characteristic of the species.

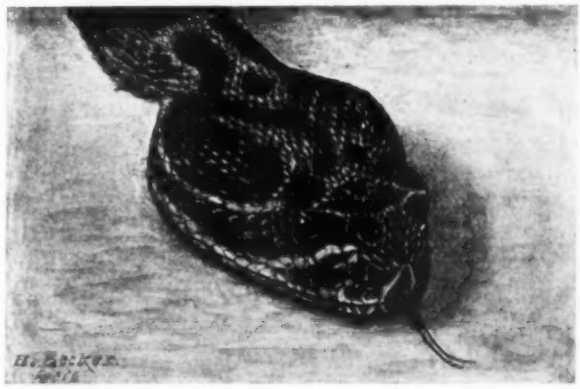

FIG. 6.

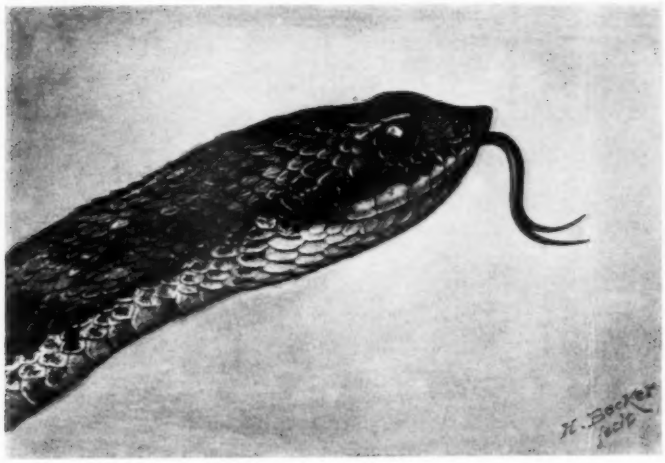

FIG. 7

Heterodon, puffing adder, hognosed viper. A harmless and valuable but threatening looking snake. The turned-up rostral plate at the end of the snout is the characteristic mark of the genus.

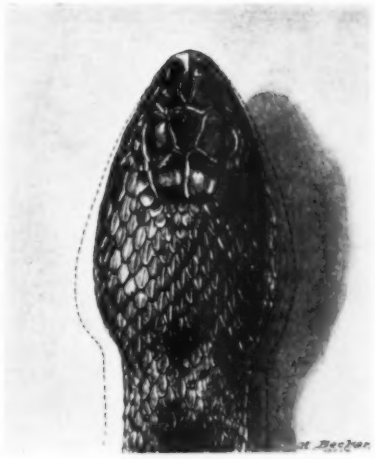

FIG. 8

This snake has the power of flattening out its head and the upper part of the neck until it bears a remarkable resemblance to a cobra.

FIG. 9

Natrix Sipedon, water snake, often erroneously called "water moccasin," and confused with the true moccasin (agkistrodon), a pugnacious but a harmless animal. The head

FIG. 10

is narrow, oval, and the vertical plate between the eyes is also narrowed in remarkable contrast with the true moccasin (see Fig. 4). There is no pit.

absence of the pit and the side-lines so characteristic of the true moccasin at once serve to differentiate the two. (Figs. 9 & 10.)

The Tropidonotus is a snake not so useful as our land-snake, as he lives on fishes and frogs, and I am willing to admit the question whether he ought not to be killed.

"Highland moccasin" is another term applied to a harmless snake which on account of the unfortunate name is condemned to be killed wherever he is found.

I trust that this demonstration with the living forms before you will impress upon you the easily recognized differences between poisonous and non-poisonous forms so that you will feel yourselves not only equipped to decide in case of accident whether the bite of a particular snake is liable to be followed by dangerous symptoms, but that you will constitute yourselves as well defenders of the harmless snakes, which are not only of great economical value but aid as well in the destruction of the poisonous forms.

ON THE CHEMISTRY, TOXICOLOGY AND THERAPY OF SNAKE POISONING.*

BY THOMAS R. BROWN, M. D.

In this portion of the country, the subject of the poison of venomous snakes and the treatment of snake-bite is rarely brought to our notice, due of course largely to the extreme rarity of the condition and the paucity of snakes of high degrees of toxicity.

Nevertheless, when one considers that in India alone the lives of more than twenty thousand human beings and sixty thousand cattle are annually sacrificed to the poisonous Ophidia, and that in Africa, Australia, Central and South America and the islands of the Indian and Eastern Pacific oceans many deaths occur annually from the same cause, it will be seen that the subject is one of sufficient magnitude to appeal to every one interested in the general subject of medicine in its broader sense.

Indeed, we have but to turn the pages of the journals devoted to bacteriology, chemistry and toxicology for the past ten years to recognize how much work is being done in this direction and how marked are the advances recently made in our knowledge of the subject.

Before going more carefully into the chemical and therapeutical side of the subject, it will be of interest to sketch briefly the morphological and zoological characteristics of the poisonous snakes and to mention the most important representatives and their geographical distribution.

The great family of snakes—the order Ophidia, has three divisions, the O. colubriformia which are innocent, the O. colubriformia venenosa and the O. viperiformia, the last two of which are poisonous and compose the Thanatophidia—a well merited name when one considers their great destructiveness.

A rapid and easy method of differentiating the innocent from the poisonous snakes is by an examination of their jaws, the harmless snake having two complete rows of small ungrooved teeth, an inner palatine and an outer maxillary, while in the venomous snakes the outer row is represented by one or more large tubular fangs firmly ankylosed to the maxillary bone.

This bone, by its movements, causes the erection or reclination of the fangs.

The maxillary bone is much smaller in the poisonous colubrine than in the innocent snake, while in the viperine snake it is reduced to a mere wedge, giving insertion to a long curved tubular fang. These fangs, when reclined, are covered by a sheath of mucous membrane, in which lie also several reserve fangs in different stages of growth, which are designed to replace the working fang, if it should be shed or lost through accident. The fangs, although described as being perforated, are in reality not so, this effect being produced by a folding of the dense, compact tooth on itself, forming either an open groove as in Hydrophidae, a complete canal as in Cobra or a still more complete tube as in Viperidae.

The poison is secreted by a conglobate racemose gland, almond-sized in the cobra, and opening by a duct into the capsule of mucous membrane, enveloping the base of the fang, the venom thence flowing into the dental canal, the same muscles which close the jaw also compressing the poison-gland and forcing the poison through the duct. At the orifice of the duct, a sphincteral arrangement of muscle fibres has been described by Fayrer in the cobra and by Weir Mitchell in the rattlesnake.

With the exception of New Zealand and the Oceanic Islands, venomous snakes are found almost all over the tropical and temperate regions of the world.

Among the more important of the poisonous snakes we have: in North America, Ancistrodon contortrix (copperhead), Ancistrodon piscivorus (water-moccasin), the many varieties of Crotalus (rattlesnake); in South America, Elaps corallinus (coral-snake), Elaps lemniscatus, Lachesis mutus and rhombata (bushmaster); in Central America, Bothrops lanceolatus (lance-snake); in the West Indies, Craspedocephalus; in Europe, Pelias or Vipera berus (adder), which is found throughout most of Europe, while in Dalmatia, Hungary and Greece we also have Vipera Redii, and in southern Europe, Vipera ammodytes (sand-viper); in Africa, Naja haje (asp), Naja haemachates, Naja noir and Cerastes, while in Australia we have Hoplocephalus curtus (tiger-snake), Pseudechis (blacksnake) and Acanthophis (deaf-adder).

Our knowledge of the Thanatophidia of India is very complete, due to the monumental work of Sir Joseph Fayrer, and it is upon the poison of these snakes that much of the best recent work has been done.

The venomous colubrine snakes of India are: of Elapidae, Naja tripudians (cobra), Ophisphagus elaps (hamadryad), Bungarus ceruleus (krait), Bungarus fasciatus (san kni); of

*Read before the Johns Hopkins Hospital Medical Society, Nov. 6th, 1899.

Xenurelaps, X. bungaroides and the various species of Callophis; and Hydrophidae, a very numerous and extremely poisonous family of sea-snakes, but, on account of their habitat, not very harmful.

The Indian viperine snakes are represented by: Daboia Russellii (chain-viper), Echis carinata (kuppur, or phoorsa-snake)—these are true vipers, while the Crotalidae or pit-vipers are only feebly represented by Trimerisuri, Peltopelor, Halys and Hypnale, which are much less poisonous than their American congeners, Crotalus, Lachesis and Craspedocephalus.

In India in 1898, 21,901 human beings died from the effect of snake-bite, and in this enormous mortality, the snakes stood in point of destructiveness in the following order: Cobra, Krait, Echis, Daboia. The toxicity of the venom, besides varying according to the species, varies markedly in the same species and variety.

Thus, the bite of the snakes of the tropics is far more dangerous than of the corresponding varieties in Europe. There is also a marked difference according to the time of year, the bite being more dangerous in the warmer season; in fact, the intensity of the venom in the same snake varies from day to day, being more on hotter days, less on cooler days; also the bites of hungry snakes are less severe than those of well-fed ones.

The poison acts most readily upon warm-blooded animals, especially if directed at once into the veins, but it is deadly to cold-blooded animals as well and to the lowest forms of invertebrate life.

Strange to say, a snake cannot poison itself or any of its species, and only slightly any other genus of poisonous snake, but innocent snakes it poisons quickly.

In some cases, especially when the victim is weak, or the poison is injected directly into the veins, death is almost instantaneous, while in other cases, death may not occur for a long while, and this may be due to a secondary infection, due to the destruction of the bactericidal properties of the blood by the venom.

As to the locality of the bite, in the great majority of cases this is on the extremities (in 61 of 65 fatal cases tabulated by Fayrer).

According to Fayrer's statistics obtained from his study of 65 fatal cases in India, 7 died under 1 hour, 8 between 1 and 2 hours after the bite, 9 between 2 and 3 hours, and 13 over 24 hours.

The symptoms of snake-bite are both local and general, these differing in relative intensity, according to the conditions of the case and the variety of snake.

Ceteris paribus, the local symptoms are the more marked, the more prolonged the case; while in cases of rapidly fatal termination, they may be practically wanting altogether.

These local symptoms differ somewhat with the variety of the snake, but, speaking generally, consist of a rapidly appearing, inflammatory, local oedema of the affected spot, followed later by more or less ecchymosis and gangrene, with or without pain, and often with the appearance of lymphangitis and local phlegmons. In the Crotalidae, where the local lesion is especially severe, besides the oedema we have extensive gangrene of the affected portion of the body; according to Fayrer, Naja (a colubrine) kills without destroying the blood's coagulability, while Daboia (a viperine) produces complete permanent fluidity.

The constitutional symptoms are to be ascribed to a poisoning of the cerebral and spinal centres, especially those of the medulla, inducing general paralysis, especially of respiration, paresthesias, and precordial pain.

Besides these we often have a marked tendency to hemorrhage from the various organs of the body (hematuria, hematemesis, etc.), diarrhea, vomiting, disturbances of vision and amaurosis, headache, dizziness and violent dyspnoea.

In cobra poisoning we have an especially rapid destruction of the respiratory functions, but the pupil of the eye is not affected, while in daboia poisoning, we have wide pupillary dilatation; there is also a greater tendency to convulsions in cobra poisoning. The cause of death may be (1), general paralysis, especially paralysis of respiration, (2), tetanic arrest of cardiac action, probably due to the action of the venom upon the cardiac ganglia, (3), a combination of these causes, (4), secondary infections of various characters, due to the destruction by the venom of the bactericidal power of the serum.

Even in the patients that recover, local paralyses in the most diverse parts of the body may persist for a long time, together with various local manifestations in the portion of the body bitten, paresthesias of various kinds, pemphigoid eruptions and pain.

Of late years, a great deal of investigation has been carried on upon the action of snake-poison, by means of animal experimentation.

Ewing has shown that the normal germicidal power of the serum is entirely lost after poisoning with Crotalus venom, and the same results have been obtained after poisoning by Pseudechis in Australia.

Many observers have shown the marked hemolytic action of the majority of snake-venoms, while Halford and Martin have called attention to the marked increase of leucocytes in the blood of animals that have recovered from snake-bite.

Brunton and Fayrer concluded from their experiments on certain of the mammals and on frogs, that cobra poison, besides paralyzing the reflex action of the cord acts upon the nerve-endings in the muscle as curare does, and Ragotzi, who has confirmed these observations, thinks that "failure of respiration is mainly brought about by this paralysis of the nerve-endings in muscle, and that the direct action of cobra-poison on the central nervous system is altogether subsidiary."

Many other interesting points regarding the physiological action of venoms have been observed, and in many cases slightly different effects have been noted, according to the species of snake from which the venom was obtained, a result not at all unexpected when we remember that there are quite marked differences in the symptoms of human beings poisoned by snakes.

As we shall see later on, however, Calmette regards the primary action of all snake-venom as the same in kind, although differing in degree, ascribing the symptoms at variance in the different cases to the presence of various albuminoid substances in the venoms, which have but little to

do with the real cause of death. Following the line of work instigated by Roux and Vaillard, in the case of tetanotoxine, Calmette and Martin, working separately, have worked out the toxic value of some of the venoms, i. e., the number of grammes of an animal (rabbit), which is killed by 1 gramme of poison introduced subcutaneously.

Calmette's results were—

Cobra, ...	4,000,000
Hoplocephalus curtus, . . .	3,450,000
Pseudechis, ...	800,000
Pelias berus, ...	250,000

while Martin placed the toxic power of the Australian venoms somewhat higher, thus:

Hoplocephalus curtus, . . .	4,000,000
Pseudechis, ...	2,000,000

The diagnosis of snake bite is, of course, easily made from the history of the case and the symptoms, and by an examination of the bitten spot.

PROGNOSIS.

As to the prognosis, this varies markedly with the country, the climate, and the species of snake. If one of the Indian snakes, Cobra, Hamadryad, Bungaris or Daboia, has inoculated its full charge of venom into its victim, the result, according to Sir Joseph Fayrer, is invariably fatal.

In America, Weir Mitchell gives a series with a mortality of 25 per cent., and another with one of 12 per cent., while Ellzey gives 15 per cent. as the usual proportion of deaths.

In Australia, it is given as about 7 per cent.

The much lower mortality in the last two countries probably depends partly upon the greater intelligence of their peoples, and their recognition of the absolute necessity for prompt treatment.

THE CHEMISTRY OF SNAKE-VENOM.

The chemistry of snake-venom should be of especial interest to Americans, because the greatest advances in our knowledge of the subject have come from the work of American investigators, especially Weir Mitchell and Reichert.

Fontana in 1781, and Prince Lucien Bonaparte in 1843, made analyses of viper-poison, and concluded that its toxicity was due to an active principle, achidnine or viperine.

Busk, from the analogy between the poison-gland of the snake and the parotid, suggested that the poison might be in some way related to ptyaline.

Weir Mitchell in 1860, found in the poison of Crotalus, (rattlesnake), two albuminoid substances, one coagulated by boiling and comparatively innocuous, the other not coagulated by boiling and poisonous, and he called attention to the "singular likeness between the symptoms of rattlesnake poisoning and those of certain maladies, such as yellow fever," an analogy already noted by S. L. Mitchell, Majendie and Gaspard, who also called attention to its resemblance to poisoning by putrefying substances.

Gautier, of Paris, ascribed the poisonous properties to a ptomaine, but this has been disproved by Mitchell, Reichert and Gibbs.

Fayrer and Brunton in 1873, showed that cobra-poison remained active after coagulation by boiling. The work, however, which has done most to clear up the chemistry of snake-venom is that of Mitchell and Reichert, the preliminary report appearing in 1886, while the full details of the work appeared later in the Smithsonian Institute Reports.

Their experiments were carried on upon the poisons of the copperhead, rattlesnake, water-moccasin and cobra.

The poison is a slightly turbid yellowish fluid, more or less viscous, always acid and having a specific gravity of between 1.050 and 1.065. Whether in the liquid or dry state, venom is soluble in water with a slight turbidity.

Venoms usually contain 25 to 50 per cent. of solids, but may contain as little as 12 per cent., or as much as 67 per cent., as noted by Martin in some of the Australian snakes.

Venoms dry rapidly at 16° to 20° C. in a desiccator, and the dried residue resembles markedly dried egg-albumin in its physical properties.

This dried venom if kept from moisture apparently keeps indefinitely, Weir Mitchell having preserved some Crotalus venom without apparent diminution of toxicity for 22 years.

In glycerine, also, venom seems to keep indefinitely.

The watery solutions of all the venoms studied, with the single exception of Crotalus adamanteus, can be subjected to the temperature of boiling water without the complete destruction of their poisonous properties. In the exception mentioned—the diamond-backed rattlesnake—the toxicity is completely destroyed by a temperature below 80° C.

The work of these two investigators showed that venom consists of at least two, and probably three, proteid-like bodies, two soluble in distilled water, and one not.

Of the two that are soluble, one does not coagulate at 100° C., and this may be obtained by boiling venom which throws down or destroys all the other proteids, and then either dialyzing or filtering.

The various reactions of this body—its positive reaction with the xantho-proteic, Adamkiewicz's and Millon's reagents, the fact that it formed no precipitate with carbon dioxide gas, ferric chloride, copper sulphate, and glacial acetic acid, and that it did form a precipitate with mercuric chloride, absolute alcohol, and potassium ferrocyanide in the presence of weak acetic acid—led them to suppose that it was a peptone and to it they gave the name of venom-peptone.

Some of its reactions were atypical, however; as, its forming a precipitate with dilute acetic acid but redissolving in excess of the reagent, its precipitation by sodium chloride, which precipitate was soluble in an excess of glacial acetic acid; these and other considerations led Wolfenden to call attention to it again and to point out that it is probably, more truly speaking, an albumose. The precipitate formed by adding water to venom was found to have the properties of a globulin, especially of paraglobulin, and was called venom-globulin; while the third proteid present, their venom-albumin, had the properties of an albumin and was considered harmless by Mitchell and Reichert. According to their experiments, the globulin acts more on the respiration, circulation and blood, tending to destroy the red blood-corpuscles, prevent coagulation, produce ecchymosis, lower blood-pressure and paralyze respiration, while the peptone (or albumose) acts more on the

tissues tending to cause oedema, putrefaction and sloughing. While most venoms contain (*a*) a proteid coagulable by heat and (*b*) a proteid or proteids not thrown out of solution by this means, it is nevertheless extremely difficult to assign exact positions to these bodies, because of the somewhat arbitrary and rather artificial means of differentiation at present in vogue, and because of the fact that many of the constituents of various venoms give atypical reactions, rendering it impossible to definitely assign them to any especial group, although the great majority of their properties may harmonize completely with those of a special class, the peptones, the proto-albumoses, etc., for example.

Recent work seems to show that cobra-poison and pseudechis-poison contain proto-albumose, while crotalus-venom seems to contain a body more closely related to the deutero-albumoses.

The amount of proteid coagulated by heat differs considerably in different species; thus, it is 24.6 per cent. in Crotalus, 7.8 per cent. in Ancistrodon, and only 1.75 per cent. in Cobra.

The whole question of the exact position of the various constituents of venom in the proteid family must be left in *statu quo* until a more definite and scientific means of differentiation of the various members is possible.

Until then, by some observers, the venoms will be regarded as made up of globulins and peptones, by others as globulins and albumoses, and by still others as albumoses alone.

A few words may be of interest as to the effect of various substances upon snake-venom, especially as it is because of these reactions that many of the therapeutic measures applied to snake-bite have been suggested.

Venoms are rendered inert by those chemical agents that destroy proteids or precipitate them in insoluble form, such as gold chloride, potassium permanganate, nitric acid and nitrate of silver; the same effect is noted with the hypochlorites, and also with more prolonged action of carbolic acid and the caustic alkalies.

Although Mitchell found that the venom of Crotalus was destroyed by gastric digestion, the venoms of Cobra, Pseudechis and Pelias berus have been shown to be unaffected thereby; while all venoms are rapidly destroyed by pancreatic digestion.

Freezing does not affect the various kinds of venoms, but they are all profoundly modified by being heated at a temperature between 75° and 80° C. Of late much attention has been called to the resemblance between the formation of snake-venom, and the production of the poisons by the diphtheria bacillus, anthrax bacillus and tubercle bacillus on the one hand, and the products of gastric and pancreatic digestion on the other.

In all these processes, various albumoses are formed, varying markedly in the degree of their toxicity, but all more or less poisonous if injected subcutaneously, while in some the process is carried still farther with the production of peptones.

As stated before, in the case of snake-poison the process of albumin-hydration probably stops short of this stage.

Another interesting point is that in some of these cases, notably gastric and pancreatic digestion, and digestion by the diphtheria bacillus, this conversion of the albumins into albumoses is brought about through the agency of a ferment or enzyme; while recently it has been suggested that in the formation of snake-venom, an enzyme may possibly take part.

TREATMENT OF SNAKE-BITE.

It is, however, regarding the treatment of snake-bite that most interest has centered during the past few years.

One has but to glance over the myriad medicaments used in this condition, drawn from the animal, vegetable and mineral kingdoms, to recognize how utterly unscientific and irrational has been the treatment of the great majority of cases, while many of the so-called remedies come directly from the realms of witchcraft and voodooism.

And yet in no condition more markedly than in this does the old adage "Bis dat, qui cito dat" hold good.

The prime object is to prevent the absorption of the poison, and if this can be done rapidly and efficaciously, we may get cures in cases in which a few minutes' delay or the wasting of time in useless procedures would inevitably result in death.

As to the best local treatment to be carried out, this varies somewhat according to the authority quoted, but the main principles are the same in all.

In the first place, a tight ligature should be applied above the bitten spot, if this is on the extremities, as we have seen is so in about 95 per cent. of cases.

As much of the poison as possible should then be removed, by scarification of the wound, excision in some cases, amputation, perhaps, if the bite is on a finger or toe and the species of snake a very dangerous one, tight bandaging from above and below toward the wound, cauterization of the bitten area, cupping or sucking the wound, although this last procedure is vigorously opposed by Fayrer and others.

About the wound should then be injected some one of the substances which experiments have shown to be rapidly destructive to the venom, usually by oxidizing it into harmless or less harmful substances.

For this purpose, potassium permanganate in solutions of from 1 per cent. to 5 per cent. as recommended by Blyth, Lacerda and Aron, and calcium hypochlorite or gold chloride as recommended by Calmette before he had developed his present method of treatment, are probably the best, although if these are not at hand, the caustic alkalies, bromine or chlorine water, carbolic, tartaric or chromic acids, tincture of iodine or even dilute solutions of mercuric chloride may be used.

Obviously all of the above-mentioned remedies are useless when the poison has once reached the general circulation, as none of these substances owe their efficacy to anything but their ability to destroy or oxidize proteids, or to form with them insoluble compounds, and would thus act equally destructively on the tissues of the body if injected into the system.

If the venom has reached the general circulation, besides hastening its elimination by washing out the stomach, and keeping the bowels and bladder well emptied (for it has been shown that the poison is, at least partially, excreted by the kidney), our energies should be devoted to counteracting as much as possible the constitutional effects of the poison, by the use of appropriate means.

Probably lives have been saved by these means, especially

after bites by the less venomous species of snakes, but according to Fayrer, all treatment is practically useless in those cases in which a member of the Indian Thanatophidia has injected its full quantity of poison into its victim, and local treatment has not been immediate. Among the remedies which have been most used to attempt to counteract the poison's constitutional effects, may be mentioned alcohol, ammonia and strychnia.

From time immemorial, alcohol has been used in this condition for its stimulating effect, while it has only been comparatively recently that ammonia has been given in any other way than by the mouth.

Due to Halford's experiments, large doses—as much as 1 drachm of the liquor ammoniae fortior—were given hypodermically, but later work has shown the utter uselessness of this drug as an antidote.

The same is largely true of strychnia, recommended first by Pringle in 1868, and more recently, in 1889, strongly advocated by Mueller, who regarded it as a true antidote if given in such large doses as to cause constitutional effects; three years later, however, indisputable figures were brought forward to show that under this treatment the mortality had not been decreased in the slightest degree.

Although useless as antidotes, both these remedies and to a less extent alcohol are probably useful in mild cases in lessening the nervous and cardiac depression after snake-bites.

Because of the marked effect of snake-venom upon the respiratory apparatus, artificial respiration has been tried in a few cases, but although the life of the man or animal is prolonged by this means, no case has been reported in which life has been saved.

Encouraged by the rapid development of the subject of serum-therapy, and by the successful results obtained in many cases, notably diphtheria and tetanus in combating by sera the effects of the toxines of bacterial growth, certain investigators, notably Calmette, at the Pasteur Institute in France, and Fraser, in Great Britain, have turned their attention to the preparation and properties of antivenomous serum, and the possibility of making use of it as a curative agent.

In 1887, however, Sewall, in the United States, first showed that a certain degree of tolerance to rattlesnake poison could be obtained by frequently feeding animals on small doses of the venom.

The results obtained by Fraser and Calmette have been quite markedly different, while their views regarding the mode of action of the antivenomous serum are almost diametrically opposed to each other, Fraser believing in the specificity of the various venoms and sera, i. e., from a serum which might immunize against one species of snake, much less good results could be expected in the case of poisoning by snakes of other species; while Calmette thinks that the active principle in the poisons of all snakes, and even of poisonous lizards and scorpions is the same, i. e., a serum which would immunize against one variety of very poisonous snake would immunize equally well against all other varieties.

All recent observers are agreed that an animal or person can be vaccinated against what would otherwise prove a fatal dose by the subcutaneous introduction of small, repeated doses of the poison.

But the reasons for this cause discussion—Fraser and Phisalix believing that the protection or immunity is chiefly due to the accumulation in the blood of an antidotal substance, which originates, at least in part, from the venom, and is normally one of the constituents of the poison itself; while Calmette, in direct opposition to this, believes that the antidotal substances are formed in the blood of the vaccinated animal itself by a certain reactive process of the organism.

Fraser, in Great Britain, and Cunningham, in India, found that the antidotal results obtained by using the serum of vaccinated and immunized animals were only of a high degree in the cases of injection of the poison of the *same* species of snake; the latter, among his other conclusions, stating that "blood-serum of vaccinated animals is efficacious as an antivenom, but only against the poison which comes from the same species of snake."

Kanthack, in this connection states that, although most snake-poisons belong to the same physiological group, and yield to the same antidote, nevertheless Calmette's serum prepared against Cobra-venom, has no effect upon Daboia-venom.

According to Fraser's experiments, it would take 300 cc. of the strongest rabbit-serum that he could produce to save the life of an average-sized man who had been bitten by one of the most venomous variety of snakes—an amount so great as to practically destroy the possibility of its practical application. Fraser, also found that the bile of poisonous snakes, and to a much less extent the bile of innocent snakes, of oxen and of guinea-pigs possessed antidotal properties, but here again the bile was much more effective against the poison of that variety of snake from which the bile was obtained; he also states that the serum of venomous serpents likewise possesses some antidotal properties, but Phisalix and Bertrand have described this as a process of vaccination, unless the blood-serum be heated to 60° C., when a true antidote is formed.

This is of especial interest because both snake-blood and snake-bile are very important remedies in the armamentarium of the native Hindoo snake-charmer and doctor, and too many well authenticated stories exist, showing immunity and cure to make it at all doubtful that these persons possess methods of treatment which are doubtless of value. The rationale of these experiments of Fraser's in regard to the antitoxic action of the bile is, of course, directly derived from the oft-repeated observation that the venom, unchanged in the stomach, is rendered rapidly inert after entering the duodenum, Fraser therefore regarding it as likely that the bile played some important part in this destruction or neutralization.

As bile is itself poisonous, Fraser isolated from the bile a non-toxic substance which had marked anti-venomous properties, and suggested that this might possibly be used for curative purposes outside the laboratory.

He also found that by feeding animals upon snake-poison, an immunity could be produced which would last 4 to 5 days; as however, at least 2 hours are required to establish this immunity after the feeding, the result of this experiment can be of no practical value.

Calmette, at the Pasteur Institute at Lille, France, has been carrying on experiments upon snake-venom exactly analogous

to those upon the toxines of tetanus and diphtheria, at first using small animals, but of late making use of larger animals, especially horses, in the preparation of his antivenomous serum. In July, 1896, his results had been attended with such success that he presented them to the Royal College of Physicians and Surgeons in London. These experiments were designed to show both the preventive and curative powers of his serum, and were as follows:—

(1) The lethal dose of cobra-venom being found to be 1 milligramme of dried substance (subcutaneously administered), which will kill a rabbit in 12 hours, or 2 milligrammes will kill in 16 to 17 minutes, 3 c. cm. of the protective serum was injected, and 6 hours later, 2 mg. of the dried venom; no symptoms occurred in these immunized rabbits, while control animals died in 16 and 17 minutes respectively.

(2) A second series was given 5 mg. of the dried venom subcutaneously, and one hour later 3 c. cm. of the antivenomous serum; all remained well.

(3) In a third series, 3 c. cm. of the antitoxine were injected one-half, one and one and a half hours after the injection of a fatal dose of the poison, and only in the last case (i. e., those injected one and a half hours afterwards) did the rabbits die.

All the animals that recovered in these experiments were perfectly well 8 days later.

The 1st experiment was designed to show the preventive, the 2d and 3d to show the curative powers of the serum.

In concluding another article on the same subject, Calmette says:—"Animals may be immunized against the venom of serpents either by means of repeated injections of doses, at first feeble, and becoming progressively stronger, or by means of successive injections of venom mixed with certain chemical substances, among which I may especially mention the chloride of gold and the hypochlorites of lime and soda; the serum of animals thus treated is at the same time preventive, antitoxic and therapeutic, exactly as is that of animals immunized against diphtheria and tetanus."

Calmette studied the venom of the following reptiles: Naja tripudians, Crotalus durissus, Bothrops lanceolatus, Naja haje, Cerastes, Bungarus fasciatus, Pseudechis, Hoplocephalus curtus, H. variegatus, Acanthophis antarcticus, Trimeresurus viridis and Trigonocephalus contortrix.

Although all these venoms have their well marked toxic peculiarities and produce their various local phenomena, nevertheless animals immunized by vaccination against very large doses of any of these venoms, resist likewise inoculations of very powerful doses of the venom of any one of the other serpents mentioned, according to Calmette.

This belief in the non-specificity of the toxines and antitoxines of snake-venom is shared by other investigators on the same subject, as Wehrmann.

In this connection it is interesting to note some of the discoveries in the field of serum-therapy that have a suggestive bearing upon this point.

Marmorek has shown that animals immunized against anthrax or tetanus furnish a serum antitoxic to snake-venom; also that dogs immunized to a high degree against rabies are capable of great resistance to snake-poison; while Calmette and others have shown that rabbits vaccinated against snake-venom, become resistant to poisoning by abrine, while those vaccinated against abrine may in turn acquire a certain degree of immunity against snake-venom, diphtheria, ricine or even sometimes against anthrax, and animals vaccinated against erysipelas or rabies may possess a serum that may even be preventive against snake-venom.

Calmette is violently opposed to the idea that there is a chemical neutralization of the toxine by the antitoxine, he regarding the immunity as due to a certain "insensibilization" of the cells in respect to the venom, which is conferred upon them for a short time by the antitoxine.

In support of this, he showed by experiment that if a lethal dose of venom and a corresponding dose of anti-venomous serum be mixed in a test-tube and injected into an animal, there are no injurious effects; while if the mixture, after standing for a sufficient length of time to bring about any chemical reaction if it should take place, be heated to 70° C. (at which temperature the antitoxic serum loses its efficacy) and then injected, death occurs as if the animal had received no antidote whatever.

Recent experiments suggest that some, at least, of the immunity after antivenomous serum has been injected, may be due to increased powers of phagocytosis towards the toxine on the part of the leucocytes.

Whatever may be our views as to the specificity or non-specificity of toxine and antitoxine, nevertheless the practical results obtained from the use of the serum give promise of great success.

For the past two and a half years, the Pasteur Institute at Lille, has been sending out serum of a high immunizing power to various parts of the world where snake-poisoning is frequent, and already has received reports showing favorable results in persons that have been bitten by the following varieties of venomous snakes: (1) Naja tripudians (cobra) of Indo-China, (2) Bungarus ceruleus (krait) of India, (3) Naja haje (asp) of Egypt, (4) Naja noir of West Africa and (5) Bothrops lanceolatus of Central America, although Martin has so far been unable to get such good results in those bitten by the Australian snakes.

It may be of interest to report one of these cases more in detail.

A boy working in the laboratory at Lille, while carelessly opening a box of newly arrived snakes, was bitten on the hand; almost immediately symptoms of violent intoxication set in, and in an hour, besides the swelling and oedema, there was insensibility of the hand and forearm, great pain in the upper arm, neck and axilla, and nausea.

12 c. cm. of the serum were injected and immediately the symptoms commenced to subside, and by the next day the boy was practically well. A woman who happened to be bitten by the same lot of snakes died in 2 hours, untreated.

Incidental to the more practical side of his work, Calmette has made a number of other interesting observations: For instance; vaccinated rabbits remain immune for a considerable length of time, losing their immunity the more rapidly, the more quickly they have become immunized; the female rabbit is able to transmit her immunity, provided the gestation takes place at the height of the immunizing period, the young

retaining this immunity for about 2 months; on the other hand the immunized male rabbit is unable to transmit his immunity to his offspring.

Even from the short account that I have given, it will be seen that decided advances have been made during the past few years, in our knowledge of the nature of snake-poison, while the number of favorable reports of the use of the anti-venomous serum makes it probable that a real antidote to snake-poison has at last been found.

In an article as brief as this, it is impossible to more than touch lightly upon the many interesting points in connection with snake-venom and snake-bite, but if any one cares to delve more deeply into the subject, I would refer him to the comprehensive articles of Mitchell, Fayrer, Lauder-Brunton, Calmette, Fraser, Kanthack, Martin, Cunningham and Wall, in whose pages he will find much that will prove of interest to the student of natural history, of toxicology, of chemistry, and of medicine and therapeutics.

THE MENSURATION AND CAPACITY OF THE FEMALE BLADDER.

OBSERVATIONS ON THE FEMALE BLADDER DILATED BY ATMOSPHERIC PRESSURE IN THE KNEE-BREAST POSTURE.*

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[The investigations here reported were undertaken by the writers upon the suggestion and with the constant aid and direction of Dr. Howard A. Kelly, of the Johns Hopkins Hospital, to whom they take pleasure in acknowledging their indebtedness.]

The interest attaching to the work is both practical and scientific, for it concerns the gynecologist even more than the anatomist.

How little is really known about the bladder is found upon a cursory reading of the surgical and anatomical text-books containing their meager and contradictory statements. The measurements and capacity of the female bladder, given in the text-books, have been determined by *post-mortem* examination, by distention to discomfort by urine (or other fluids), and by other inexact methods, which have given imperfect and often contradictory results.

The methods employed by the writers in their investigation differ from those heretofore employed in essential and important respects:—1st, all measurements have been made on living women, in most cases with the bladder either perfectly healthy, or so slightly changed from the normal as not to affect the accuracy of the results; 2d, all examinations have been made with the women in the knee-breast posture, with the rectum, vagina and bladder all (with a few exceptions), dilated with air, according to the method so well known from the writings of Kelly. With all cases thus placed under similar conditions for the examination, the chief sources of avoidable error were removed, and relative measurements could be made and certain averages and standards found. It was, of course, impracticable to estimate the variations of intra-abdominal pressure in different cases or to fix upon a standard of this force, but repeated examinations of the capacity of the bladder in the same case showed that this force was nearly uniform. Although this force may be assumed to vary in different cases and thus to influence the capacity of the bladder when it is opened to the entrance of the outside air, still we believe that this variation is far less important than the variation due to individual tolerance or irritability to fluid distention, the method previously most generally employed in determining the capacity of the bladder. It was found, moreover, that by this method of air dilatation, no discomfort* was felt by the woman, and consequently no resistance, either voluntary or involuntary, was offered by her, thus adding to the uniformity of the conditions of observation. On the contrary, it was found that distention by fluid to discomfort was subject to the peculiar and varying irritability or tolerance of the subject, and thus gave no uniform basis of comparison.

The work was undertaken primarily to afford to the gynecologist some additional information on the size, shape, position, internal measurements, and capacity of the bladder, and incidentally to furnish the anatomist with some of the same data.

Had the study been made primarily from the anatomical viewpoint, it might have been better to have made the observations on the bladder alone distended, without the distention also of the vagina and rectum. But we have found that while the dilated vagina and rectum have a certain influence on the shape and position of the dilated bladder, they influence only slightly its air capacity.†

The chief points investigated were, 1st, the average atmospheric distention capacity of the female bladder, and 2d, its actual internal measurements, from the internal urethral orifice to certain chosen points on its walls.

For the purpose of the first study, the woman was put in the knee-breast posture and the three pelvic cavities were each allowed to dilate with air. A closely fitting catheter was then introduced into the bladder, attached at its

*Abbreviated report of the paper read before the Johns Hopkins Medical Society, December 4, 1899. The full report will appear in the Journal of the American Medical Association, December 16, 1899.

*The patients never complained of discomforts from the distended bladder while in the knee-breast posture. After rotation to the dorsal position, however, they usually felt some slight discomfort, if they were not under anæsthesia, and were instructed, before being rotated, to refrain from any expulsive effort.

†This last statement needs confirmation, as our observations on this point were few.

external end to a long, soft rubber tube. The rubber tube was closed by a clamp and the woman was then rotated carefully by assistants from the knee-breast into the dorsal position. The rubber tube was then introduced into a deep vessel of water and from below upward into an inverted glass graduated cylinder completely filled with water, and was held pointing upward in this position by an assistant. The clamp on the tube was then released, and the entire air content of the bladder was expressed by the ordinary gynecological bimanual method, with one hand exerting pressure on the bladder externally from the abdominal wall and with the other hand pressing at the same time upon the bladder from within the vagina or rectum.

The air thus expressed was collected in the glass cylinder, displacing from above downward an equal amount of water, and the amount was read off on the graduated cylinder, thus determining the exact air capacity of the bladder.

To test whether all the air was thus removed from the bladder, a special instrument was devised, consisting of a double-barreled catheter (Figs. I and II), by which the bladder, after bimanual expression, was flushed with boric solution, and any air remaining in it was forced out and collected for measurement. It was thus found that bimanual expression had been effectual and complete, and practically all the air in the bladder had been removed.

In the 25 women examined the average bladder capacity by atmospheric dilatation was found to be 303 cc, individual cases ranging from a minimum of 160 cc. to a maximum of 545 cc.

Measurement was also made in 22 cases of the fluid content of the bladder, boric solution being used for this purpose. On anæsthetized cases the solution was introduced through the double-barreled catheter until it overflowed through the upper barrel, on the cases without anæsthesia, until discomfort was caused to the woman. The average fluid capacity was thus found to be 429.7 cc., varying in individual cases from a minimum of 210 cc. to a maximum of 840 cc. The fluid capacity of the bladder was thus found to be more than one-third greater than the air capacity, a difference that would be expected, because of the elasticity of the bladder-walls under the increased pressure of fluid.

With reference to the influence of anæsthesia on the capacity, the following table has been arranged:

	Atmospheric Capacity.		Fluid Capacity.	
With anæsthesia,	306.7 cc.	(average 17 cases.)	449.6 cc.	(average 15 cases.)
Without "	295.0 cc.	(average 8 cases.)	387.1 cc.	(average 7 cases.)
	303.0 cc.	(average 25 cases.)	429.7 cc.	(average 22 cases.)

From these figures it is seen, as might be expected, that the average capacity of the bladder for both air and fluid is somewhat greater with than without anæsthesia, explained, doubtless, by the relaxation of the bladder-walls during anæsthesia. The above figures tend also to show that this difference is greater with fluid than with atmospheric distention, due to the more varying irritability of the bladder, without anæsthesia, to fluid distention.

The influence of child-bearing on the capacity of the bladder is shown in the following table:

	Atmospheric Capacity.	Fluid Capacity.
Nulliparous,	318.8 cc. (average 13 cases.)	464.5 cc. (average 11 cases.)
Parous,	291.2 cc. (average 12 cases.)	395.0 cc. (average 11 cases.)

The explanation of these figures, showing the greater capacity of the bladder of nulliparæ, is doubtful, and it may be that it is purely accidental, due to the limited number of cases observed. We would suggest, however, that it may be due to the greater elasticity of the bladder of the nullipara, influenced both by her younger average age and by the fact that her bladder and the surrounding tissues have not suffered injury and undergone sclerotic changes as the result of the pressure of the gravid uterus. The influence of age is shown in the fact that the average age of the women who had borne children was 36 years, and of the nulliparous women only 26 years.

The second chief object of this study was to gather some statistics on the internal mensuration of the bladder under atmospheric dilatation in the knee-breast posture. The value of such measurements to the gynecologist is apparent, but they have not before been accurately ascertained.

The distance of certain points from the internal urethral orifice was measured. The points chosen were:

(1) The *vertex*, or summit, the most prominent and distant point in the concavity of the upward and anterior bulging of the ventral wall, placed usually well above the reflection of the peritoneum and the departure of the urachus; (2) the most prominent and distant point in the upward and dorsal bulging of the *posterior wall*. This point is found a few centimeters above the peritoneal reflexion, and is usually opposite the end of the cystoscope when it is held in the axis of the patient's body. Quite frequently, however, the cystoscope must be directed more posteriorly to bring this point into view; (3) the point of greatest outward bulging in the *left lateral wall*; and (4) the point of greatest outward bulging in the *right lateral wall*.

These four points are not scientifically fixed points, but in actual work are found to be sufficiently clearly indicated for practical purposes of identification and description (Fig. III).

The average measurements obtained for these four points were, to

Vertex.....	7.14 cm.	Left lateral wall..	6.70 cm.
Posterior wall.....	5.77 cm.	Right lateral wall.	5.92 cm.

Taking the measurements separately for nulliparous and for parous women, the averages are found to be:

	Vertex.	Posterior wall.	Left lateral wall.	Right lateral wall.
Nulliparous (average, 13 cases)	7.43 cm.	5.75 cm.	7.03 cm.	6.12 cm.
Parous (average, 12 cases) ...	6.83 cm.	5.79 cm.	6.35 cm.	5 72 cm.

The greater average internal dimensions of the bladder of nulliparæ, here shown, correspond to the greater capacity for air and fluid, as already pointed out, and may be explained in the same way.

The asymmetry of the dilated bladder shown by the unequal lateral measurements is of interest. In sixteen cases the left lateral measurement is greater than the right, the reverse is true in six cases, and in three the left and right internal lateral

Fig. I.

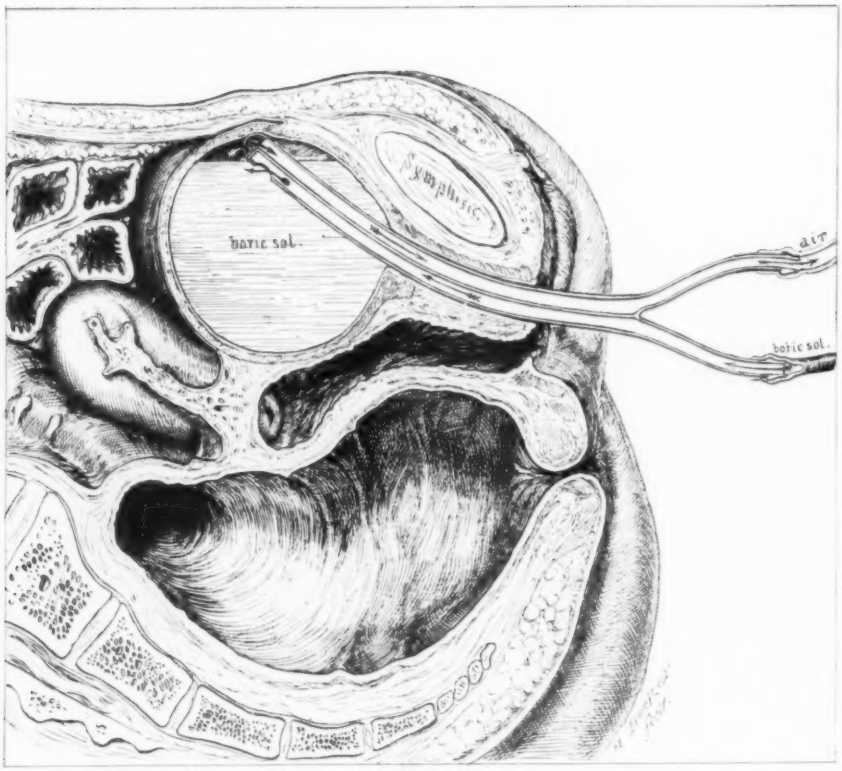

FIG. II.

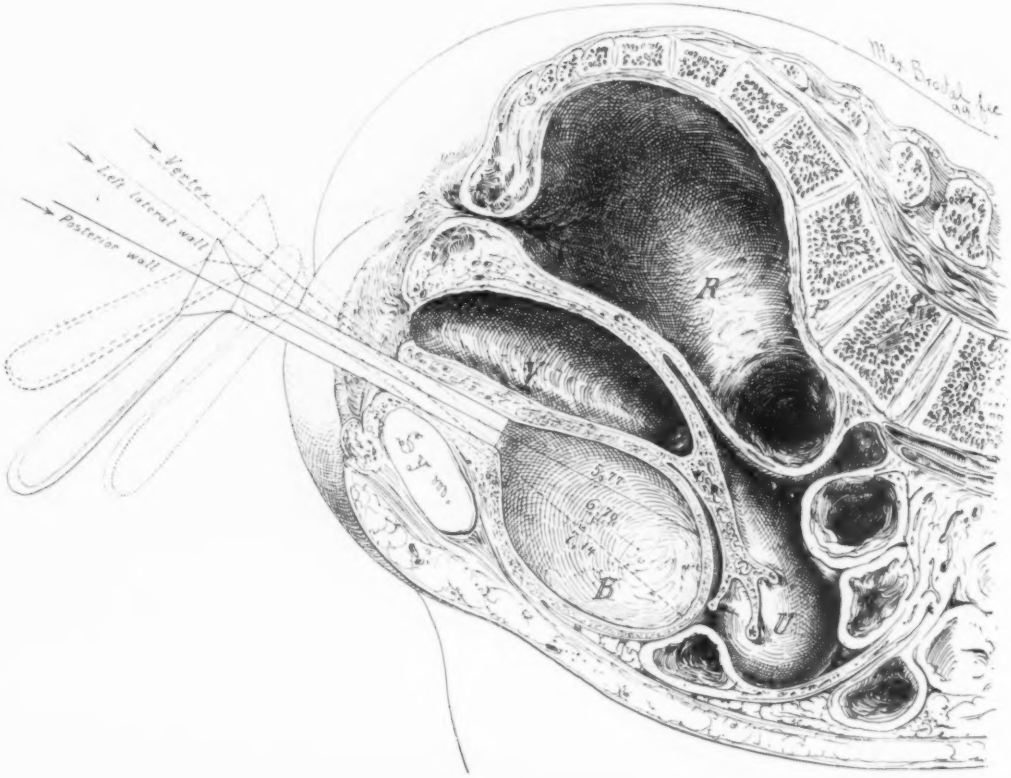

FIG. III.

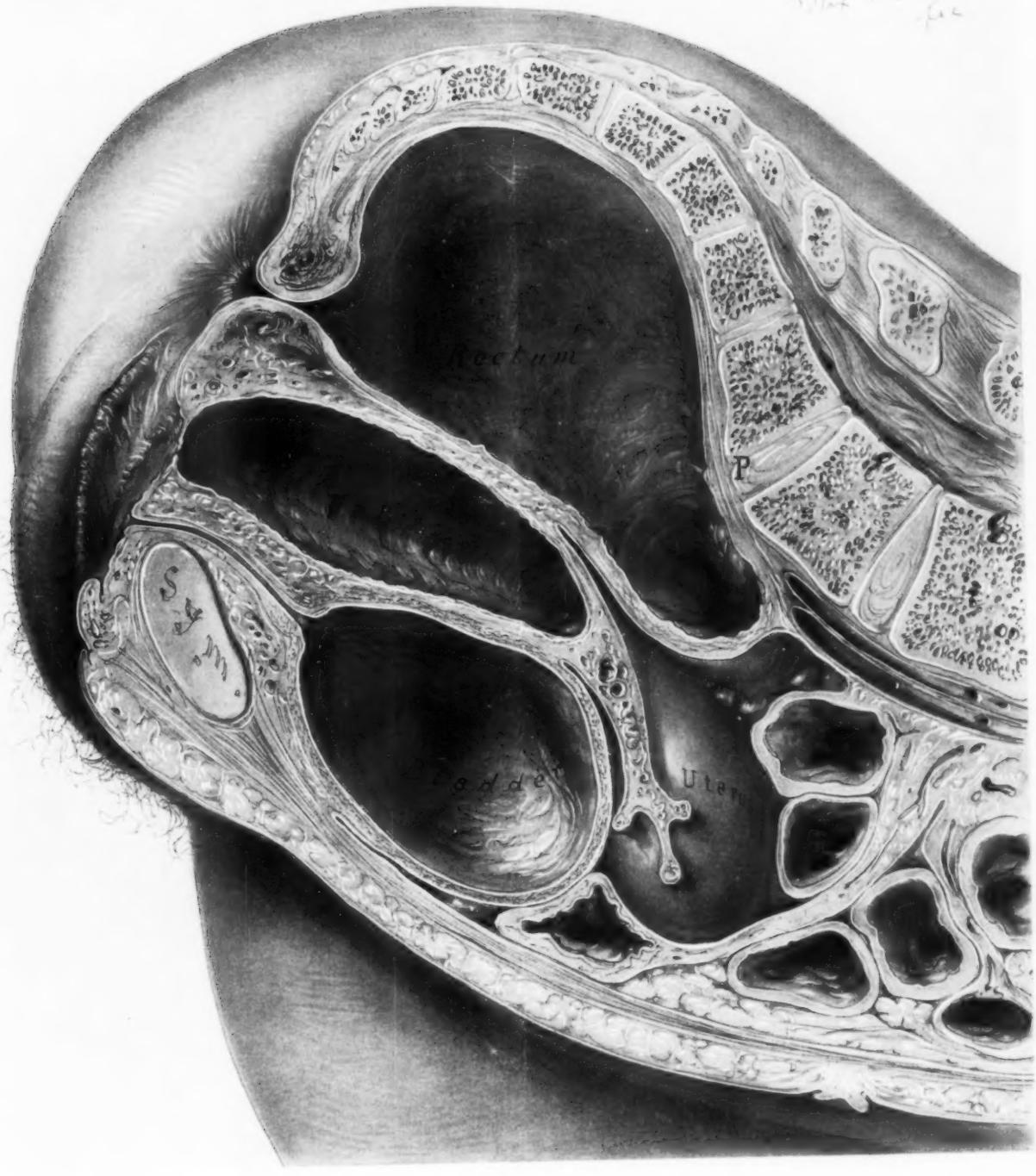

Fig. IV.

measurements are equal. The occasional asymmetrical position of the bladder has been noted by anatomists, but never before has this asymmetry been recorded in so large a proportion of cases. This tendency of the bladder to be placed more to the left than to the right, at least when the patient is in the knee-breast posture with the three pelvic cavities dilated with air, may be explained by the fact that the rectum in women is found more commonly on the right than the left in the pelvis, and thus the distended rectum tends to displace the bladder toward the left. Our observations on the position of the rectum in women are directly opposed to the usual statements of the text-books of anatomy. Mr. Max Brödel,* artist to the gynecological department of the Johns Hopkins Hospital, whose observations on the anatomy of the organs of the pelvic cavity have been exact and extensive, informs us that his own experience confirms our observation on this point.

Another factor producing some slight asymmetry of the dilated bladder is the fact that the uterus† is usually placed somewhat to the left of the median line and encroaches upon the left upper posterior quadrant of the bladder, as is well shown in Fig. IV. The influence of this factor is to lower the point of greatest outward bulging of the left lateral wall, point (3), so that it is found to be at a lower level than point (4) on the right lateral wall.

It was found that the same patient examined repeatedly by the same method gave, as a rule, nearly uniform measurements, the variations being slight.

All cases were free from any constricting clothing at the time of the examination, and the rectum had been emptied by cathartic or enema before the examination.

With the patient in the knee-breast posture, and the rectum, vagina and bladder all dilated by atmospheric pressure, it was found that the true pelvis was always completely occupied by these three organs and that the bladder and the uterus tended to rise upward and forward. In multiparæ the uterus was found to be displaced so far upward and forward that its fundus could be felt within a few centimeters of the umbilicus (Fig. IV).

The ballooning of the rectum and vagina before the bladder was allowed to fill with air, was found to be of great importance to the ease of the examination of the ureteral orifices, in the fact that the dilated vagina and rectum press from behind upon the base of the bladder, thus bringing the trigonum and ureteral orifices forward and into easy view of the speculum. *Neglect of this point and failure to first allow the rectum and vagina to dilate are accountable in large measure for the difficulty found by many gynecologists in catheterizing the ureters.*

The ureteral orifices were seen on or were indicated by a slight elevation of the mucous membrane, the *mons ureteris* of Kelly, but in some cases in young nulliparous women the ureteral opening was indicated by a small round black point which was never observed in older women who had borne children.

The bladder as a whole, when dilated with air and observed during operation within the pelvic cavity (from abdominal section) was found to be ellipsoidal in form, flattened somewhat in its antero-posterior diameter, and increased transversely. The transverse diameter was always the greatest measurement.

A mathematical calculation of the cubic content of an ellipsoidal viscus of the dimensions of the bladder corresponds closely with the actual air capacity obtained by expression.

The average length of the urethra in seventeen cases was 3.3 cm., the shortest urethra measuring 2.7 cm., and the longest 4.2 cm.

It is hoped by the writers that the measurements and observations above recorded, though limited to twenty-five cases, may prove of interest and service especially to the gynecologist, by affording a certain amount of carefully ascertained facts about the relative measurements and topography of the female bladder under air dilatation in the knee-breast posture.

DESCRIPTION OF FIGS. I, II, III, IV.

FIG. I—Represents the double-barreled catheter and attachments, used for determining the residual air in the bladder, after bimanual expression.

FIG. II—Median section, dorsal position, showing the double-barreled catheter in position in the bladder, boric solution entering through the lower chamber and forcing the air out through the upper chamber.

FIG. III—Median section, knee-breast posture, showing the pelvic cavities dilated with air, and the cystoscope in position for obtaining the measurements of the vertex, posterior wall, and left lateral wall.

FIG. IV—Median section, knee-breast posture, showing the anatomical relations of the pelvic organs when the rectum, vagina and bladder are dilated with air. (Multipara.)

*To Messrs. Brödel and Becker, of the Johns Hopkins Hospital, we wish to express our indebtedness for their beautiful drawings from which Figs. II, III and IV have been made.

†This observation is also opposed to the statements of some text-books of anatomy, and is confirmed by Mr. Brödel.

SUMMARIES OR TITLES OF PAPERS BY MEMBERS OF THE HOSPITAL AND MEDICAL SCHOOL STAFF APPEARING ELSEWHERE THAN IN THE BULLETIN.

HOWARD A. KELLY, M. D. Exploration of the Abdomen as an adjunct to every Celiotomy.*

I had occasion on several instances some sixteen years ago to make a post-mortem examination and to remove various viscera which I was desirous of inspecting, through the vaginal vault in women and the perineum and rectum in men. These experiences showed me that it is easy to reach all the viscera through an incision as far as possible from the centre of the abdomen, large enough to admit the forearm, and suggested the propriety or rather the necessity of making a somewhat analogous investigation of all the abdominal organs in the living subject every time the abdomen is opened.

The routine examination of the abdominal and pelvic viscera in all celiotomies, where it does not endanger the life of the patient,

*A more extended consideration of this subject appears in the *Medical News*, December 16, 1899.

will commend itself to a surgeon for a number of excellent reasons, some of which are the following:

First, as abdominal diseases are commonest in middle life, the period when most of our celiotomies are performed, it is practically certain that the coincidence of two or more entirely independent diseases will be discovered in some instances by means of this examination.

Again, there is a constant association between certain abdominal affections and affections elsewhere, in the form of a mutual interdependence, either from the propagation of disease, as in the case of cancer, sarcoma and tuberculosis; or mechanically, where the effects of pressure are manifested near to or at a distance from the seat of disease, as in the case of pelvic tumors or inflammation obstructing the vascular, the urinary or the alimentary channels. These secondary conditions often in their initial and curable stages may be brought to light by the method of investigation here advocated.

Moreover, such an examination, if negative, gives both operator and patient a much more comfortable assurance that the convalescence will be without interruption, as well as the satisfaction of realizing that there is no visceral affection in progress which may in the near future tend to shorten life or to impair health.

The following diseases are most likely to be found in such a routine examination: appendicitis, hernia (either inguinal or umbilical), hydroureter, disease of the omentum, pyloric cancer, movable kidney, enteroptosis, cancer of the liver, perihepatitis, gall stones.

In making the exploration extreme care must be taken to maintain asepsis by thoroughly sterilizing the arm or, better still, by wearing a rubber glove with a long sleeve reaching as far as the elbow. If the area in the immediate neighborhood of the incision is so septic as to require the use of drainage, the operator had best forego the more extended examination. The best position of the patient for the examination is either lying flat on the table or with the pelvis slightly elevated. The structures are examined in an order which must vary with the location of the incision. When the abdominal opening is made low down over the middle of the pelvis, I commonly follow some such routine as this: After carefully noting the condition of each pelvic viscus, uterus, tubes and ovaries, bladder and rectum, I look at the inguinal and umbilical ring and if there exists a hernia I proceed to sew it up at once from the inside of the abdomen. The next point of importance requiring examination is the vermiform appendix.* This should be removed if it shows any traces of previous inflammation. Then follows the inspection of the ureters, of great importance in gynecological operations. Every surgeon should be thoroughly familiar with the ureteral landmarks. The position of the transverse colon and the stomach is noted on account of the frequency of enteroptosis.

The operator now introduces his forearm and palpates both kidneys, noting their presence, size, form and mobility. A stone in the renal pelvis is readily felt. After the kidney, the liver is palpated, its apparent size, the regularity of its surface, any adhesions, which when present indicate perihepatitis, being noted, and most important the gall bladder is explored. I next put my index finger in the foramen of Winslow and trace the common duct down for several centimetres, feeling for stone.

The spleen, the pancreas, retroperitoneal lymph glands, and finally the abdominal portion of the aorta are palpated in order.

There are in general three classes of cases to which this extended examination may be applied.

First. Those in which there has been no reason to anticipate disease of any other organ and the examination is made simply as a routine procedure whenever it adds nothing to the gravity of the situation.

Second. Those cases in which, on opening the abdomen, contrary to expectation, no disease is found near at hand. I recall a case* of this sort in which I made an incision over the appendix, and, finding no appendicitis, enlarged the opening and discovered a gall stone within a ruptured gall bladder; also an instance in which gall stones were believed to be present, but on finding the diagnosis at fault, I introduced my arm through the enlarged incision and came upon a large hematoma of the ovary.

Third. The group of cases in which there exists a definite percentage of chances that the disease discovered at the time of operation is complicated by the affection of some other organ neighboring or remote.

* The method I follow in reaching the various organs is detailed in loc. cit.

REID HUNT. Direct and Reflex Acceleration of the Mammalian Heart with some Observations on the Relations of the Inhibitory and Accelerator Nerves.—*American Journal of Physiology*, II, pp. 395-470.

Experiments on dogs and cats showed that in these animals the center of the accelerator nerves is almost always in a condition of tonic activity and that the normal rate of the heart is determined in part by this tonic activity. Section of the accelerator nerves sometimes causes the heart to become irregular; this is especially true if the irritability of the heart is low. The most important functions of the accelerators seem to be connected with their tonic activity.

Long-continued stimulation of the accelerators causes fatigue and sometimes even death of the heart. If the vagi are in tonic activity, or if they are stimulated simultaneously with the accelerators, the latter cause less fatigue of the heart.

Reflex acceleration might be caused either by increasing the activity of the accelerators or by decreasing the tonic activity of the vagi. The latter was found to be the usual if not the exclusive method. Reflex acceleration was never obtained after section of the vagi although the accelerators were intact, but was readily obtained if the vagi were intact although the accelerators were cut.

It seems very probable that most cases of rapid heart action (voluntary acceleration, acceleration during muscular exercise and after the administration of drugs, the rapid heart of paroxysmal tachycardia etc.) so far as they are dependent upon the extracardiac nerves, are largely due to diminution of the tonic activity of the vagi and not to a stimulation of the accelerators; in paroxysmal tachycardia especially the entire course of the acceleration is markedly different from the effects of stimulating the accelerator nerves in animals.

W. S. BAER, M. D., P. M. DAWSON, M. D., and H. T. MARSHALL, M. D. Regeneration of the Dorsal Root Fibres of the Second Cervical Nerve within the Spinal Cord.—*Journal of Experimental Medicine*, January, 1899.

LEWELLYS F. BARKER, M. B. Progress of Neurology.—*Philadelphia Medical Journal*, January 28 and February 4, 1899.

——— A Case of Glioma of the Lower Cervical Region of the Spinal Cord Producing a Total Transverse Lesion, in which there was Spasticity of the Lower Limbs and Persistence of the Deep Reflexes. A Study of a Peculiar Form of Degeneration (Degeneratio Micans) met with in this Case.—*American Journal of the Medical Sciences*, Vol. 117.

SIMON FLEXNER, M. D. Some Points in the Pathology of Syringomyelia.—*American Journal of the Medical Sciences*, Vol. 117.

——— Hodgkin's Disease.—*American Journal of the Medical Sciences*, Vol. 118.

THOMAS B. FUTCHER, M. B. Lipemia in Diabetes Mellitus.—*The Journal of the American Medical Association*, Vol. 33.

——— A Critical Summary of Recent Literature Concerning the Mosquito as an Agent in Transmission of Malaria.—*American Journal of the Medical Sciences*, Vol. 118.

* For description of cases, see loc. cit.

HENRY HARRIS, M. D. Preparation of the Abdomen for Operation. —*American Journal of Obstetrics*, Vol. 40.

HOWARD A. KELLY, M. D. A New Method of Treating Complete Tear of the Rectovaginal Septum by Turning Down an Apron into the Rectum and by Buried Suture through the Sphincter Muscle. (Illustrated.)—*Medical News*, Vol. 75.

—— New Handle and Grip for Scissors in Plastic and Other Work.—*American Journal of Obstetrics*, Vol. 40.

—— Operation for Complete Tear of the Perineum.—*American Journal of Obstetrics*, Vol. 40.

—— The Reflux of Air into the Ureters through the Air-Distended Bladder in the Knee-Breast Posture.—*American Journal of Obstetrics*, Vol. 40.

—— Some New Instruments to Facilitate the Operation of Myomectomy.—*American Journal of Obstetrics*, Vol. 40.

—— The Use of the Renal Catheter in Determining the Seat of Obscure Pain in the Side.—*American Journal of Obstetrics*, Vol. 40.

J. H. MASON KNOX, JR., PH. D., M. D. On Supra-arterial Epicardial Fibroid Nodules.—*The Journal of Experimental Medicine*, March, 1899.

JOHN BRUCE MACCALLUM, M. D. A Contribution to the Knowledge of the Pathology of Fragmentation and Segmentation, and Fibrosis of the Myocardium.—*The Journal of Experimental Medicine*, May-July, 1899.

FRANKLIN P. MALL, M. D. Liberty in Medical Education.—*Philadelphia Medical Journal*, April 1, 1899.

JOSEPH LONGWORTH NICHOLS, M. D. A study of the Spinal Cord by Nissl's Method in Typhoid Fever and in Experimental Infection with the Typhoid Bacillus.—*The Journal of Experimental Medicine*, March, 1899.

EUGENE L. OPIE, M. D. A Case of Hæmochromatosis. The Relation of Hæmochromatosis to Bronzed Diabetes.—*The Journal of Experimental Medicine*, May-July, 1899.

WILLIAM OSLER, M. D. An Acute Myxœdematous Condition, with Tachycardia, Glycosuria, Melæna, Mania and Death. *The Journal of Nervous and Mental Diseases.*

—— In Memoriam William Pepper. *Philadelphia Medical Journal*, March 14, 1899.

—— The Cavendish Lecture on the Etiology and Diagnosis of Cerebrospinal Fever.—*The Boston Medical and Surgical Journal*, Vol. 141.

—— The Clinical Features of Sporadic Trichinosis.—*American Journal of the Medical Sciences*, Vol. 117.

—— The Diagnosis of Typhoid Fever. A Discussion at the New York State Medical Association, October 25, 1899.—*New York Medical Journal*, Vol. 70.

OTTO G. RAMSEY, M. D. The Early Use of Purgatives after an Abdominal Section.—*American Journal of Obstetrics*, Vol. 40.

H. O. REIK, M. D. The Sterilization of Instruments with Formaldehyde.—*Philadelphia Medical Journal*. February 4, 1899.

W. S. THAYER, M. D., and JESSE WILLIAM LAZEAR, M. D. A Second Case of Gonorrhœal Septicæmia and Ulcerative Endocarditis with Observations upon the Cardiac Complications of Gonorrhœa.—*Journal of Experimental Medicine*, January, 1899.

J. WHITRIDGE WILLIAMS, M. D. Anti-Streptococcus Serum.—*American Journal of Obstetrics*, Vol. 40.

—— A Case of Spondylolisthesis.—*American Journal of Obstetrics*, Vol. 40.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Monday, November 20, 1899.

The meeting was called to order by the President, Dr. Henry M. Thomas.

Cases Illustrating Forms of Pigmentation of the Skin.—Dr. OSLER.

CASE I. *Addison's Disease.*—A man, aged 40, was admitted a few days ago, complaining of weakness, pain in the stomach and bowels, and a gradual pigmentation of the skin. He had been a man of good habits and of good health until five years ago, when he began to have gastric trouble, chiefly regurgitation of the food. About four years ago he began to have pains below the costal margin and radiating over the abdomen. They came on in paroxysms three or four times in the course of the year, and were sometimes accompanied by vomiting. During this time his complexion grew steadily darker, and within the past twelve months his condition has grown worse. He has paroxysms of sudden pain, chiefly about the right costal margin, followed by vomiting, headaches and at times great prostration. These paroxysms are preceded by twitchings of muscles of the limbs, especially of the arms, so marked that he has not been able to write. After these spells the prostration is extreme and at times he has hardly been able to move in bed for nearly a week. Each spell leaves him weaker and he has not done a day's work for a year. The vomiting has averaged once a day during the past year, and yet his appetite is excellent. He has never had any diarrhœa. He looks somewhat emaciated and has lost fifteen or twenty pounds. The face, hands, and more particularly the body, are uniformly pigmented. There is slight pigmentation of the mucous membrane of the gums. His pulse is slow but not feeble and the blood count shows 6,000,000 red cells.

The combination of symptoms presented by this man is characteristic of Addison's disease, yet the case is somewhat peculiar. There is no history of tuberculosis; there is no reaction to tuberculin, and the duration of four or five years is rather unusual, the disease being as a rule very much shorter. Asthenia, such as he describes, a prostration of such a degree as to render him unable to turn in bed, or even to move, is most characteristic, and in fact the diagnosis may sometimes be made on the asthenia and gastro-intestinal symptoms without pigmentation.

CASE II. *Hæmachromatosis* (?).—This lad presents a still more remarkable and very much more unusual condition. This boy came here in April, 1896, with malaria and looking as if he had had a malarial cachexia of long duration. He had not been ill long, but looked so bronzed and pigmented

that we commented upon it in the history. We could not reasonably explain this pigmentation, but thought he must have had malaria longer than shown by his history. He came to the hospital again in February, 1897, with tertian malaria, and he was this time even more pigmented, but I forget whether at that time we noted any enlargement of the liver. In September, 1899, he appeared again with an acute psoas abscess, and at that time we found that he had an enlarged liver and spleen. Meantime we had been educated at the Society by Dr. Eugene L. Opie on the subject of hæmachromatosis, and this case corresponds in certain features with that remarkable disease. He has had no asthenia, no feebleness of pulse or muscular weakness, and no trace of gastro-intestinal disturbances, though those features have been sought for very carefully.

His pigmentation, as you see at present, is extreme, being quite marked in the face, and there is a little pigmentation of the mucous membrane at the margin of the lips. This bronzing has grown gradually deeper, so that he looks to-day more bronzed than he was in September. The liver is moderately enlarged and can be felt two or three finger breadths below the costal margin. The edge of the spleen is only just palpable. There is no sugar in the urine. Very possibly the condition is that of hæmachromatosis.

We have had a case of this remarkable disease which is characterized by progressive pigmentation of the skin and internal organs with hypertrophic cirrhosis of the liver, sclerosis of the spleen and finally of the pancreas with the pancreatic form of diabetes. The majority of these cases have been described under the name of Bronzed Diabetes. The disease was fully described by Dr. Opie in the last number of the *Journal of Experimental Medicine.*

Case III. *Melanoderma in chronic myocarditis.*—We can not say that all cases of progressive pigmentation of the skin are either due to hæmachromatosis or to Addison's disease, for there are certain conditions, particularly certain forms of chronic heart disease, some cases of chronic nephritis, etc., in which pigmentation of the skin develops and increases, and occasionally is accompanied even by pigmentation of the mucous membranes.

This man has been under observation for several years, having been admitted first in January, 1891, and nine times since, always with the same symptoms—shortness of breath, extreme irregularity of the pulse, dilated heart and sometimes with slight swelling of the feet. He has chronic myocarditis and progressive pigmentation of the skin. His face has deepened in color and the general surface of the body is pigmented. There is no pigmentation of the mucous membranes and though he has had extremely feeble and irregular pulse, he has not had the asthenia which characterizes Addison's disease. He has no enlargement of the liver or spleen. A piece of skin was removed for examination by Dr. Opie, but we have not yet received his report.

The diagnosis between the pigmentation of the skin in Addison's disease and in hæmachromatosis can be readily made, as the pigment in the latter case is an iron containing one and is found in abundance in the skin and also in the cells of the sweat-glands.

Case IV. *Melanoderma in Anæmia Splenica.*—Dr. Osler then referred briefly to a fourth cure of pigmentation of the skin, at present in the private ward. The young man had enlarged spleen and anæmia of the chlorotic type and gradual pigmentation of the skin. Several of the cases of splenic anæmia which had been under observation of late years have presented an extreme degree of melanoderma.

A Case of Purulent Leptomeningitis Associated with Acute Endocarditis due to Infection with the Micrococcus Lanceolatus.—Dr. Futcher.

The specimens which Dr. Barker will show were interesting on account of the number of complications that developed during the clinical course of this case in the wards. The patient came into the hospital November 5, complaining of shortness of breath. There was nothing special in the past history of the patient, nor in the family history. Seven years ago the patient had an attack of rheumatism and he gave a history of severe headache lasting about six weeks previous to admission and so intense that he was totally incapacitated for work. During this time he had frequent chills believed to be of malarious origin. Two weeks before admission he developed severe shortness of breath, cough and expectoration of bloody sputum. Later he had marked œdema of the feet and some general anasarca. On admission he was in marked distress, quite dyspnœic, somewhat cyanotic and presented the physical signs of aortic and mitral insufficiency. The sputum was tenacious and tinged with bright blood, such as one sees in cases of lung infarction. There was an area of consolidation over the middle lobe on the right side with typical tubular breathing and a pleuritic friction rub extending into the axillary region. The heart symptoms persisted for several days, the temperature during this time being irregularly elevated, running as high as 101.5°. During his illness he complained of severe pain in the region of the spleen, and splenic infarction was diagnosed. Nothing of special importance happened until the night of November 12, when his temperature arose 7.5 degrees inside of eight hours. The next morning he was semi-unconscious and it was found that he had distinct rigidity of the arms and legs with exaggeration of the knee-reflexes. On the 16th Doctor Osler suggested lumbar puncture and 15 cc. of slightly turbid fluid were obtained, which showed typical lanceolate diplococci in large numbers, but none of them intracellular. This of course clinched the diagnosis. Two days later he developed a conjunctivitis, and smears from this secretion also showed the typical lanceolate diplococci. About 24 hours before death there was complete steaminess and opacity of the right cornea. He died on November 18, the temperature being 106.4° at the time of death.

It was suspected that we would find at autopsy chronic endocarditis, with a supervening acute endocarditis, an infarction of the middle lobe of the right lung as well as of the spleen and a pneumococcus meningitis.

Exhibition of the Organs.—Dr. Barker.

The organs from this case are of more than ordinary interest. The autopsy confirms in almost every point the clinical diagnosis. The body 170 cm. long was that of a strong individual, moderately emaciated. Rigor mortis was

well marked and there was livor mortis in dependent parts. The peritoneal cavity was dry, and free from old adhesions. The diaphragm on the right side reached as high as the fourth intercostal space; on the left side to the fifth rib. There were a few firm old adhesions at the posterior margin of the left pleural cavity. On the right side the costal and visceral pleuræ were slightly adherent, especially over the middle lobe and the middle part of the upper lobe. The adhesions on the right side are all recent and fibrinous. This cavity is free from old fibrous adhesions. The pericardium aside from one old patch of thickening shows no alterations. The heart is much enlarged, weighing 418 grammes. In the right atrium the valve of the coronary sinus is remarkably developed, forming a large, thin, multiply perforated membrane. The cavities of the heart are somewhat dilated and the walls are thickened. On opening the left ventricle the bicuspid valve is found to measure 10.4 cm. in circumference. At the base of the anterior cusp of the valve on the atrial surface at its right extremity is a bulging area measuring 12 x 7 mm. and protruding for a distance of from 3–4 mm. above the surface of the valve, showing the endocardium before it. On puncture yellowish-green pus exuded and the swelling disappeared. The posterior cusp is shorter than normal, but otherwise shows no alterations. On the ventricular surface of the anterior cusp close beneath the posterior semilunar valve of the aorta there is a small ulcerated area, the margins and base of which are necrotic. Fibrin is deposited upon the surface of the ulcer. The introduction of a probe shows direct continuity with the abscess described on the atrial surface of the valve. In the aortic semilunar valves there are both old and recent changes. The old alterations consist in the main of fusion of the adjacent edges of the posterior and right semilunar valves. The edges of the two valves corresponding to this fusion are very much thickened and the lunulæ have disappeared. The lunula on the left side of the posterior cusp is intact and normal, while that on the right side has disappeared, and the valve is much thickened and retracted below it. The left lunula of the right semilunar valve is present, but considerably thickened, while the right lunula of this valve has entirely disappeared and the main body of the valve close to it is thickened. The adherent valves are, in the region of the adhesion practically immobile, owing to formation of new connective tissue and partial calcification. This change in the valve must have caused a relatively high degree of insufficiency and a slight stenosis. In the left aortic semilunar valve there has been apparently no chronic change except for slight thickening of the edge of the lunula. On the ventricular surface of the valve, however, there is distinct evidence of recent acute alteration. Here one sees a large flat ulcer, 1 cm. in diameter, to which flakes of fibrin are adherent. On the aortic surface of the same valve there is also an area of necrosis with deposition of fibrin. The trabeculæ carneæ are more prominent than normal in the left ventricle. The endocardium, especially over the septum, is slightly roughened and granular. At the root of the aorta there are some reddish and yellowish patches, elevated, which on section, are of a yellow color and opaque. The myocardium is in general pale brown in color, and no areas of scarring myocarditis are visible to the naked eye. The left coronary artery shows a few patches of arteriosclerosis in the descending ramus and also in the circumflex ramus. The right coronary artery also contains patches of sclerosis.

In the middle lobe of the right lung there is a large hæmorrhagic infarction surrounded by an area of fresh consolidation. Coverslips from the consolidated area show large numbers of pneumococci. The acute fibrinous pleurisy apparently had its origin by extension from the consolidated region of the lung. The left lung is emphysematous along its anterior margin and at the apex. There is only moderate coal pigmentation. Both lungs show the typical changes of chronic passive congestion.

The kidneys show a slight degree of chronic diffuse nephritis, the capsule being somewhat adherent and the cortical substance diminished in amount. Frozen sections also show the changes of acute parenchymatous degeneration. In the organs of the abdomen there is little remarkable with the exception of the changes of chronic passive congestion and the existence of a small hæmorrhagic infarction at the inferior extremity of the spleen.

On removal of the calvarium the dura mater was found to be unusually adherent, but otherwise normal. The superior sagittal sinus contains in its anterior part a few decolorized blood-clots, evidently *ante-mortem*, loosely adherent to arachnoidal granulations which project into the lumen of the sinus. At the base of the brain the arachnoid is raised from the underlying pia by a collection of pus several millimetres in depth. The pus contains large numbers of encapsulated pneumococci and many empty capsules. The very purulent area extends from a point 10 cm. in front of the optic chiasm backwards as far as the middle of the ventral surface of the cerebellum, the breadth of the area averaging as much as 8 cm. Pus is also abundant in the Sylvian fossa concealing the blood-vessels. While the process is most marked at the base of the brain, it is by no means confined to it, for if one looks at the lateral surfaces they are found also to be more or less involved. The deeper sulci on the lateral surface contain visible pus, but over the gyri themselves very little pus is observable, although the vessels of the pia arachnoid are everywhere intensely congested.

On opening the spinal canal a small hole was found in the dura in the lumbar region corresponding to the lumbar puncture made during life. The internal surface of the dura is smooth and glistening and aside from slight capillary ectasis shows no alterations. The subarachnoid cavity of the dorsal surface of the lumbar part of the spinal cord contains in many places accumulations of pus. The areas where pus is visible vary in size, some being much larger than others. The whole dorsal surface of the cord is more or less bathed in yellowish green pus. The pus is especially abundant in the thoracic part of the cord, but there is also a considerable amount in the cervical region. The pial blood-vessels are everywhere markedly injected. The spinal nerves do not appear to be especially involved in the inflammation, but along the cerebral nerves pus can be easily followed. It was especially abundant in the course of the cochlear and vestibular nerves. The possibility of middle-ear disease was of course suspected, but both ears

were carefully opened and no evidence of a primary process there could be found. Pus could be followed along the left optic nerve into the orbit and the eye when removed showed a general purulent inflammation. Radiating from the point of entrance of the ophthalmic artery yellowish lines could be followed along the vessels between the retina and the chorioid coat. The vitreous body and the crystalline lens were turbid from infiltration with pus, coverslips from which showed large numbers of pneumococci and no other micro-organisms. The iris, cornea and conjunctiva were also acutely inflamed.

ANATOMICAL DIAGNOSIS: *Leptomeningitis cerebrospinalis purulenta; panophthalmitis purulenta acuta; endocarditis ulcerosa maligna; endocarditis valvularis chronica; hypertrophia et dilatatio cordis; arteriosclerosis aortæ et aa. coronariarum; infarctio pulmonis dextræ; pneumonitis et pleuritis acuta; pleuritis chronica adhæsiva; congestio chronica passiva; infarctio lienis; degeneratio parenchymatosa renum; nephritis chronica diffusa incipiens.*

As has been said the pneumococcus was found in the pulmonic infarction and the consolidated lung about it; in the purulent inflammation of the eye; in the purulent exudate in the brain and spinal cord, and in the ulcers and abscess on the valves of the heart. Dr. Harris recovered the coccus in cultures. It is of interest to trace the probable sequence of events in the case. The chronic valvular endocarditis doubtless dates back to the attack of rheumatism from which the patient suffered seven years ago. Resulting from the old endocarditis and aortic insufficiency came hypertrophy of the heart accompanied, doubtless at times, by dilatation of its chambers. The chronic passive congestion of the lungs and other organs is obviously the result of the cardiac disease. It is probable that the chronic circulatory disturbance and the changes produced by it in the organs, made the individual unusually susceptible to infection. The question arises which of the several local infections from which the man suffered was primary. The clinical evidence is in favor of a primary endocarditis with complicating meningitis. It seems to me impossible to say, however, from the autopsy findings alone which is primary, the meningitis or the endocarditis. The infarction of the spleen is easily explicable when one remembers the ulcerative endocarditis in the left heart. The infarction of the lung can scarcely be referred to the heart directly, for there is no acute endocarditis on the right side of the heart, nor did the cavities of the heart contain thrombi of any kind. The most probable explanation seems to me to be that of the thrombi which formed in the superior sagittal sinus of the brain and were very loosely adherent, one passed into the venous current and by way of the right heart entered the pulmonary artery as an embolus leading to the pulmonary infarction. Pneumococci being in the blood, the pneumonic infiltration in the periphery of the infarct is easily accounted for. It is not to be forgotten, however, that there is much evidence in favor of the view that pulmonary thrombosis can occur as the result of local processes in the walls of the pulmonary artery without the occurrence of embolism. The whole subject is fully discussed in the article on thrombosis and embolism in Clifford Albutt's System of Medicine.

NOTES ON NEW BOOKS.

The Nervous System and Its Constituent Neurones. By LEWELLYS F. BARKER, M. B., Tor., Associate Professor of Anatomy in the Johns Hopkins University; Assistant Resident Pathologist to the Johns Hopkins Hospital. (*D. Appleton & Co., New York*, 1899.)

In 1897 Dr. Barker began a series of anatomical papers in the *New York Medical Journal* for the purpose of presenting some of the most important recent discoveries relating to the nervous system. He had little idea at the commencement of his work that these papers would form a book of more than a thousand pages. For nearly two years articles on the anatomy of the nervous system appeared from Dr. Barker's pen, at irregular intervals, until the writer realized that should his method be continued, an end of his work could hardly be attained. The intense activity of investigators in this domain makes the task of keeping abreast of their discoveries a difficult one. Dr. Barker decided, therefore, that a book would be the best form in which to present the results of his labors. He accepts the neurone concept without hesitation and makes it the foundation of his work.

The book is divided into six sections, of which the last comprises much more than half of the entire volume. In these sections are considered the history of the development of the neurone concept, the external morphology of the neurones, the histogenetic relations of the neurones, the neurone as the unit in physiological and pathological processes, and the grouping and chaining together of neurones in a complex nervous system like that of man and the higher animals.

In criticizing any book it is only fair to the author that we should constantly bear in mind the object he has had before him. Dr. Barker's book is chiefly a review of the work of others, but it is a review by a man of excellent critical ability who knows how to sift the good from the bad and to present in strong light the important features of many valuable papers. It is not a book containing merely the results of Dr. Barker's original investigations, although throughout the work the author's hall-mark is found, and in many places a statement of his views on the opinions quoted from others. We find also evidences that the microscope has been diligently employed by him, and that a very large amount of literature has been carefully studied.

Dr. Barker begins his book with a brief account of the imperfect knowledge of the nervous system existing fifty or sixty years ago, and shows how, step by step, information has been gained. It is interesting to review this history. We are too prone to accept the achievements of the past without recognition of the laborious methods by which they were made possible. We find a brief account of the rise of the silver method—but not the fall, as some overzealous writers would have us believe—and the methylene-blue method of Ehrlich, that has never been so extensively employed as its value warrants, is described. Dr. Barker is one of the strongest defenders of the neurone concept. The independence of the neurone, he says, has apparently, at least so far as embryonic tissues are concerned, had its complete anatomical justification, and even granting the claims of Held, Apáthy and Bethe, the general validity of the doctrine of the individuality of the neurones would not be affected.

Van Gehuchten is said to have found changes in the terminal nucleus of a sensory nerve after sensory axones of the first order were cut—similar changes to those that occur in motor neurones. This is true, but it should be mentioned that Van Gehuchten himself later questioned the correctness of his former interpretation. The findings of Marinesco in regard to this question are said by Dr. Barker to have been curiously enough misinterpreted. Marinesco however, seems to have been correct, for Van Gehuchten has demonstrated by the silver method that the cells of the posterior nucleus of the vagus send their axis cylinders towards the periphery of the medulla oblongata, and that this posterior nucleus is motor. We need more evidence before we can accept the statement that

changes similar to those in motor cells occur in the cell bodies of the second sensory neurones after diversion of the axis cylinders of the peripheral sensory neurones.

A brief but excellent account of Apáthy's work is given. We feel that a great truth has been only partially revealed to us when we study Apáthy's writings. Whether or not Apáthy's and Bethe's statements will force us to abandon the neurone theory, the future alone can show. We must acknowledge that this concept depends on the results obtained by various methods, and that it seems impossible to explain certain findings by any other theory at present known to us; and yet the writer of this review would hardly care to say with Dr. Barker that the validity of the neurone concept has been so firmly established that it can never be utterly overthrown. The downfall of the Roman empire seemed impossible at one period, and some of the best-established theories have fallen before the revelations of science.

Dr. Barker gives Nissl's classification in as simple a form as possible. The students of medicine—for whom in part this book is written—who will carry these types in their memories do not exist in every medical school. Dr. Barker's résumé of the views held in regard to the nerve-cell is excellent. We should hardly expect that everything of importance written on this subject could be crowded into a few pages of a text-book, but the author has performed the task he set for himself; he has given a brief résumé of the work of others and an expression of opinion regarding the relative value of this work, and possibly he has given more than most students will easily grasp.

The chapters on embryology are concise and contain the most important facts. The description of the metameres is of especial value at this time, on account of the importance attributed to them in disease by certain writers. The metameres appear in the embryo as sharply defined masses in the mesoderm lateral from the chorda dorsalis and the medullary tube. A spinal nerve with its sensory and motor roots, spinal ganglion and portions of the medullary tube to which it belongs, represents a neurotome. Brissaud has recently explained many cutaneous diseases and other conditions by a theory based on the metameres. The description which Dr. Barker gives of the shifting of the diaphragm and the explanation thereby of how an abdominal muscle is supplied by a cervical nerve, are very interesting.

Dr. Barker, in his chapters on the physiology of the neurone refers to facts which are almost incomprehensible; such, for example, as the production by the activity of the neurones of chemical compounds of a degree of complexity scarcely approached elsewhere on this planet; or the preservation of memory in certain cells notwithstanding the constant changes of structure, which he expresses in the words "Dauer in Wechsel." We have in this latter statement a mystery the human mind is unable to solve. Marinesco has recently written on this subject. According to his view, the duration of a nerve-cell is as long as the duration of the organism. * * * "C'est grâce à cette fixité des cellules nerveuses que la vie psychique est possible. C'est cette propriété remarquable qui nous explique également la transmission héréditaire de certaines propriétés vitales de l'organisme. Si, en effet, les cellules nerveuses devaient sans cesse se trouver en voie de multiplication, il serait bien difficile de pouvoir expliquer la persistance remarquable de nos souvenirs, de la formation de nos idées; la transmission de l'immunité, etc." A nerve-cell may change, may grow, but there is still a "Dauer in Wechsel."

It may be permissible to correct a slight error that has crept into Dr. Barker's book. In referring to a paper by Dejerine and Spiller, Dr. Barker says that these writers contest the extension of endogenous fibers into the median triangle of Gombault and Philippe (p. 458); on the contrary, the words of Dejerine and Spiller are: "Le triangle médian de MM. Gombault et Philippe contient—à côté de fibres endogènes dont l' existence est très probable—un grand nombre de fibres exogènes ou radiculaires."

The central pathways of cranial nerves have only in slight extent been determined. This is well shown by a study of the vestibular nerve, although more knowledge has been acquired regarding the cochlear nerve. Even the most recent studies leave much to be desired. The acoustic pathway has been a favorite subject with Dr. Barker and he has written on it previously.

Dr. Barker believes that the consensus of opinion is that the function of the posterior columns of the cord is the conduction of the so-called muscular sense and not of tactile sense. In regard to tactile sense we are more uncertain. He believes that all the centripetal fibers in the inner capsule occupy the posterior part of the pars occipitalis. This view, however, is disputed by Dejerine. He agrees with Dejerine and some other investigators in teaching that most of the sensory neurones are interrupted in the optic thalamus. Little is known of the central neurones of the gustatory conduction paths, and Dr. Barker dismisses the subject in a few lines. If we compare the space allotted to the discussion of these fibers with that given to the discussion of the central olfactory tract, we realize that the latter pathway is exceedingly complex and that it is among the most difficult structures of the central nervous system to understand.

All through the book references are made to Miss Sabin's reconstructions of tracts and nuclei. This is a recent and valuable mode of studying the central nervous system, and Miss Sabin has been one of the most active workers in this field. We have an excellent proof of the value of this work in the picture of the lower olive given on page 958. A picture like this conveys a better idea of the convolutions of this body than can be obtained from a study of microscopical sections. This reconstruction demands time and care, and we read therefore with some surprise the numerous references to the extensive work Miss Sabin has accomplished.

The chapter on the central visual neurones is a very interesting one. The inaccuracy of the term "optic nerve" is pointed out, but no attempt at change—and we think the omission is wise—has been made. "Optic nerve" does not lead to the confusion that "ascending root of the fifth nerve" causes. We are somewhat surprised that the work of Vialet on the optic tracts and centers receives such scant recognition. The pupillary fibers of the optic tract and optic nerve are mentioned, but nothing is said of the extraordinary statements of Massaut concerning degeneration of these fibers.

All the important recent literature on the centers of the "upper facial" and "lower facial" nerves is not given. The investigations of Marinesco and Van Gehuchten show that the "upper facial" nucleus is a part of the pontile facial center and not a part of the oculomotor center. Marinesco has published within the past few months a second paper on this subject containing the results of his latest investigations and confirming his former statements in their most essential details.

Too much praise of the form in which this book has come from the press cannot be given. The volume is a beautiful example of the printer's art. The illustrations are numerous and well chosen. The author's style is fluent, and it is evident that Dr. Barker is a master of the English language. This book is one of which we may well be proud, and it can be said with truth that it contains the results of the most recent scientific investigations on the nervous system. We regret that the sympathetic system is passed over in silence, and express the hope that this deficiency may be remedied by the appearance of a separate monograph. W. G. S.

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The Treatment of Pelvic Inflammations Through the Vagina. By William R. Pryor, M. D. With one hundred and ten illustrations. 1899. 8vo. 248 pages. W. B. Saunders, Philadelphia.

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The Medical Department of the Johns Hopkins University was opened for the instruction of students October, 1893. This School of Medicine is an integral and coördinate part of the Johns Hopkins University, and it also derives great advantages from its close affiliation with the Johns Hopkins Hospital. The required period of study for the degree of Doctor of Medicine is four years. The academic year begins on the first of October and ends the middle of June, with short recesses at Christmas and Easter. Men and women are admitted upon the same terms.

In the methods of instruction especial emphasis is laid upon practical work in the Laboratories and in the Dispensary and Wards of the Hospital. While the aim of the School is primarily to train practitioners of medicine and surgery, it is recognized that the medical art should rest upon a suitable preliminary education and upon thorough training in the medical sciences. The first two years of the course are devoted mainly to practical work, combined with demonstrations, recitations and, when deemed necessary, lectures, in the Laboratories of Anatomy, Physiology, Physiological Chemistry, Pharmacology and Toxicology, Pathology and Bacteriology. During the last two years the student is given abundant opportunity for the personal study of cases of disease, his time being spent largely in the Hospital Wards and Dispensary and in the Clinical Laboratories. Especially advantageous for thorough clinical training are the arrangements by which the students, divided into groups, engage in practical work in the Dispensary, and throughout the fourth year serve as clinical clerks and surgical dressers in the wards of the Hospital.

REQUIREMENTS FOR ADMISSION.

As candidates for the degree of Doctor of Medicine the school receives:

1. Those who have satisfactorily completed the Chemical-Biological course which leads to the A. B. degree in this university.

2. Graduates of approved colleges or scientific schools who can furnish evidence: (*a*) That they have acquaintance with Latin and a good reading knowledge of French and German; (*b*) That they have such knowledge of physics, chemistry, and biology as is imparted by the regular minor courses given in these subjects in this university.

The phrase "a minor course," as here employed, means a course that requires a year for its completion. In physics, four class-room exercises and three hours a week in the laboratory are required; in chemistry and biology, four class-room exercises and five hours a week in the laboratory in each subject.

3. Those who give evidence by examination that they possess the general education implied by a degree in arts or in science from an approved college or scientific school, and the knowledge of French, German, Latin, physics, chemistry, and biology above indicated.

Applicants for admission will receive blanks to be filled out relating to their previous courses of study.

They are required to furnish certificates from officers of the colleges or scientific schools where they have studied, as to the courses pursued in physics, chemistry and biology. If such certificates are satisfactory, no examination in these subjects will be required from those who possess a degree in arts or science from an approved college or scientific school.

Candidates who have not received a degree in arts or in science from an approved college or scientific school, will be required (1) to pass, at the beginning of the session in October, the matriculation examination for admission to the collegiate department of the Johns Hopkins University, (2) then to pass examinations equivalent to those taken by students completing the Chemical-Biological course which leads to the A. B. degree in this University, and (3) to furnish satisfactory certificates that they have had the requisite laboratory training as specified above. It is expected that only in very rare instances will applicants who do not possess a degree in arts or science be able to meet these requirements for admission.

Hearers and special workers, not candidates for a degree, will be received at the discretion of the Faculty.

ADMISSION TO ADVANCED STANDING.

Applicants for admission to advanced standing must furnish evidence (1) that the foregoing terms of admission as regards preliminary training have been fulfilled, (2) that courses equivalent in kind and amount to those given here, preceding that year of the course for admission to which application is made, have been satisfactorily completed, and (3) must pass examinations at the beginning of the session in October in all the subjects that have been already pursued by the class to which admission is sought. Certificates of standing elsewhere cannot be accepted in place of these examinations.

SPECIAL COURSES FOR GRADUATES IN MEDICINE.

Since the opening of the Johns Hopkins Hospital in 1889, courses of instruction have been offered to graduates in medicine. The attendance upon these courses has steadily increased with each succeeding year and indicates gratifying appreciation of the special advantages here afforded. With the completed organization of the Medical School, it was found necessary to give the courses intended especially for physicians at a later period of the academic year than that hitherto selected. It is, however, believed that the period now chosen for this purpose is more convenient for the majority of those desiring to take the courses than the former one. The special courses of instruction for graduates in medicine are now given annually during the months of May and June. During April there is a preliminary course in Normal Histology. These courses are in Pathology, Bacteriology, Clinical Microscopy, General Medicine, Surgery, Gynecology, Dermatology, Diseases of Children, Diseases of the Nervous System, Genito-Urinary Diseases, Laryngology and Rhinology, and Ophthalmology and Otology. The instruction is intended to meet the requirements of practitioners of medicine, and is almost wholly of a practical character. It includes laboratory courses, demonstrations, bedside teaching, and clinical instruction in the wards, dispensary, amphitheatre, and operating rooms of the Hospital. These courses are open to those who have taken a medical degree and who give evidence satisfactory to the several instructors that they are prepared to profit by the opportunities here offered. The number of students who can be accommodated in some of the practical courses is necessarily limited. For these the places are assigned according to the date of application.

During October a select number of physicians will be admitted to a special class for the study of the important tropical diseases met with in this region.

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